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STONES IN THE COMMON AND HEPATIC BILE DUCTS*

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IN eighteen hundred patients operated upon for gall stones in the Clinic, the common and hepatic ducts have been opened, explored for stones and drained in five hundred and thirty-one cases, approximately in thirty per cent of this group. Common duct stones have been found and removed in two hundred and fifty-eight cases, approximately fifteen per cent of the cases. Of these two hundred and fifty-eight cases, it has been possible to obtain satisfactory follow-up data in two hundred and twenty-one. The mortality for the two hundred and twenty-one followed proved common duct stone cases was 7.6 per cent as compared with a mortality of 3.8 per cent for the entire eighteen hundred unsegregated cases of cholelithiasis upon which we have operated, exactly twice as high. The mortality in all cases having had common duct exploration was 4.3 per cent. We have lost only one patient following a common duct exploration which did not have stones in the ducts. The fact that in this series stones were found in the gallbladder in the presence of common and hepatic duct stones in ninety-six per cent of the cases, the fact that by increasing the number of ducts which we now explore, we have markedly increased the number of cases in which we have found common duct stones and the fact that jaundice, the sign upon which the diagnosis of common duct stones used to hinge, was absent both in the history and at the time of operation in thirty-nine per cent of these two hundred and twenty-one cases, makes it desirable, we believe, to analyze these two hundred and twenty-one cases of surgically proved common and hepatic duct stones, to stress again the fact that particularly based upon older indications for exploration of the ducts, it is very easy to leave common and hepatic stones in operations for cholelithiasis and to discuss some of our experiences with common and hepatic duct cases.

It is interesting to note that in our series, common and hepatic duct stones were found four times more often in women than in men due, no doubt, to the predominating number of females who have the condition as compared with males.

TABLE 1

(INCIDENCE)

Males	43	19.4%
Females	178	79.6%
	221	

TABLE 2

AGE

Years	No.	
11-20	1	(17 years)
21-30	14	
31-40	25	
41-50	49	
51-60	60	
61-70	49	
71-80	7	
81-90	1	(84 years)
	206	

15 cases, age not given

15 or 7.4% were under 30 years of age

These figures are of interest and value chiefly as relates to the fact that 7.4 per cent of these surgically proved cases were under thirty years of age. One does not usually think of stones being present in the common and hepatic ducts in relatively young people, yet when one notes that we have removed stones from the main bile ducts in a girl of seventeen and that of the whole series, one out of every thirteen surgically proved cases was under thirty years of age, it is obvious that common duct stones are not confined to middle-aged and aged.

TABLE 3

SYMPTOMATOLOGY

A. Duration	
Less than 1 month	13%
1 month to 1 year	33%
1 year to 5 years	26%
5 years to 10 years	12%
11 years to 20 years	11%
Over 20 years	4%

Forty-six per cent had symptoms of less than 1 year's duration

One notes, in table 2, the successful removal

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of common duct stones in a patient of eighty-four years, a doctor's mother and seven cases between seventy and eighty years, but we wish to state emphatically that such operations at this age attended as they are with such a high risk rate, have never been done as duct explorations but as last resort measures in the presence of persisting or recurring colic or jaundice associated with cholangitis as evidenced by marked temperature reactions.

A. The fact that forty-six per cent of the cases had had symptoms for less than one year is, we believe, a tribute to the intelligence of the patients and doctors of this community and an indication that the attitude of the past against which we have for several years inveighed is changing, that is, the tendency both of the patient and family physician to permit numerous attacks of gallstone colic to occur before deciding for surgery.

TABLE 3

B. Right upper quadrant colic
172 or 80%

B. Right upper quadrant colic was present in one hundred and seventy-two of the cases or eighty per cent of the total. In twenty per cent, it was absent. When one appreciates that in twenty per cent of the cases in which common duct stones were found and proved by surgical removal, colic was not present, it is obvious that if we do not wish to leave common duct stones after cholecystectomies in patients who will later bother us and be reoperated on with higher risk rates, we must explore more common and hepatic ducts and upon different criteria than has often been the case in the past.

TABLE 3

C. Chills and Fever
9 or 4.2%

C. Chills and fever were present in these two hundred and twenty-one proved cases with common and hepatic duct stones in a much lower percentage than one would expect, due we believe, to the fact that such a large percentage of the cases were operated upon early, due to the high percentage of ducts explored and due to the considerable number of cases in which the stones were small, not causing obstructive symptoms and probably having existed but for a relatively short period of time. One can, we believe, properly assume that a considerable number of patients in whom unsuspected stones were removed from the common duct at the time of cholecystectomy could have been saved from the dangers and difficulties associated with later deep jaundice and associated cholangitis.

In reviewing our gall-stone cases, we have made three different studies of the percentage of cases with surgically proved stones in the main bile ducts who were not and had never been jaundiced and it is of interest to note these percentages in the sequence of their determination. In the first series, thirty-seven per cent were without jaundice, in the second thirty-nine per cent and in this series, thirty-nine per cent. We have said before and again call attention to it that in over a third of the patients in whom stones have been found and removed from the common duct, jaundice was

TABLE 3

D. Jaundice, present in the history or physical examination 129 cases or 61%
Absent in both history and physical examination 81 cases or 39%
(10 cases not given)

at no time present. This also helps to account for the low percentage (4.2 per cent) of serious cholangitis as seen in table 3C. These figures indicate that jaundice as an indication to explore the common and hepatic bile ducts is unreliable, and that were explorations limited to those cases in which jaundice was present or had occurred in the history, common duct stones might have been left behind after cholecystectomy in eighty-six out of the two hundred and twenty-one cases.

TABLE 4

X-Ray Findings

Out of 95 Cases of Proved Common or Hepatic Duct Stones with X-Rays

Intravenous dye positive for stones in the gallbladder	70
Oral dye positive for stones in the gallbladder	10
Flat plate positive for stones	13
Intravenous dye negative for stones in the gallbladder	2

X-ray diagnosis for gall stones was accurate in 98% of the cases x-rayed

Forty-three per cent of the entire series of two hundred and twenty-one cases had gallbladder x-rays

This is about the usual x-ray finding in anyone's hands and is convincing evidence of the accuracy of x-ray diagnosis in cholelithiasis.

TABLE 5

Accuracy of Duodenal Drainage in 32 Cases

Duodenal drainage positive for stone	30 cases
Duodenal drainage negative for stone	2 cases

In thirty-two cases in which duodenal drainage was employed as a diagnostic measure in patients with questionable cholelithiasis, the positive factor being calcium or cholesterol

crystals in the drainage sediment and in all of which cases common or hepatic duct stones were demonstrated at operation, thirty cases were positive for stones and two cases negative for stones. This is another available diagnostic measure in doubtful cases of common duct stones and has its greatest value in those cases where common duct stones are suspected after a cholecystectomy has previously been done and, therefore, x-ray diagnosis not available. It is in these cases that it is so desirable to have some preoperative aid in deciding for or against reoperation and exploration of the common duct.

TABLE 6

END RESULTS IN 141 FOLLOWED CASES

1. Excellent	1-10 years	94.5% of the cases
2. Probable recurrent common duct stones		5.5%
3. Operative mortality		7.6%

Sixty-four per cent were followed from one year to ten years

The cases in the second group have not all been proved definitely as having recurrent common duct stone. Cases are included in this group which have had colic following operation suggestive of common duct stone but there are several which we have not been able to bring to reoperation.

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Sixty-four per cent of the cases or one hundred and forty-one cases have been followed from one to ten years.

An excellent result (freedom from pain and jaundice) has been obtained in 94.5 per cent of these cases.

Probable recurrent or persisting common duct stones has occurred in 5.5 per cent of the cases.

Not all of the cases in this latter group have been proved by operation to have common duct stone but even though some of the cases may not have recurrent or persistent stones, included in this group are all cases with colic after removal of common and hepatic duct stones. This is an extremely good showing as to end results and much better than I had expected would be the case because of the uncertainties at least up to recently, of complete removal of all duct stones.

TABLE 7

1. Stones in both the gallbladder and bile ducts	212 or 96%
2. Stones in the biliary ducts only, gallbladder being negative	9 or 4%

The fact that stones existed coincidentally in the gallbladder and in the common and hepatic ducts in two hundred and twelve cases, 96 per cent, speaks in favor of the fact that whatever causes stones in the gallbladder tends likewise to result in stones in the bile ducts. When one realizes, however, that following removal of the gallbladder and removal of the stones from the common and hepatic ducts, there have been but 5 per cent recurrent stones, there is at least a suggestion of what we have always thought to be true, that long-standing infection of the gallbladder results in eventual infection of the common and hepatic ducts which is relieved by removal of the gallbladder, drainage of the duct and removal of its stones.

With the introduction of the Bakes ampulla dilators by the passage of which the sphincter of Oddi can be so dilated that any average-sized common and hepatic duct stones will pass into the duodenum, it was hoped that the danger of leaving behind small common duct stones was overcome.

We have now employed these dilators in a good many cases and with no intention to be critical of what appears to be a real advance in common duct surgery, but with a desire to be helpful and frank about our own experience, we have to report that in two cases where we have widely dilated the ampulla, gas bacillus infection resulting fatally has occurred apparently ascending from the duodenum through the dilated ampulla along the bile channels. Autopsies were performed in both of these cases so that there can be no question about the cause of death and there seems little question about the origin of the infection. This experience must make us at least cautious in dilating these sphincters widely so that regurgitation of duodenal drainage into the ducts can occur. In a personal communication, Dr. Arthur Allen reports that this has never occurred in over two hundred dilatations of the sphincter at the Massachusetts General Hospital.

It is disappointing to report these two unfortunate deaths because there are so many advantages to dilatation of the sphincter of Oddi. When a large dilator can be passed through the sphincter one is quite certain that any stones at the ampulla have been removed and that if small ones are left, they will be washed down through the widely dilated duct by the secretory pressure of the bile within the ducts. One cannot, however, fail to appreciate the possible dangers of the method in the presence of these two proved fatalities and it would be wrong not to call everyone's attention to them.

These figures of the percentage of common and hepatic ducts explored have been published several times before. To these figures, we have added the percentages explored and the percentages of stones found for the years nineteen thirty-three, nineteen thirty-four and for the present year up to September, nineteen thirty-five, as graphic evidence of the incidence of stones discovered in the main bile ducts by

widening the indications for exploration of the ducts.

As the result of this fairly large experience with common and hepatic duct stones, we have arrived at some quite definite convictions.

There has been at least an impression that adding exploration of the main bile ducts to cholecystectomy, adds definitely to the operative risk of gallstone operations. Granted that the surgeon has had sufficient experience with common duct surgery, we do not believe that this is so. We are further convinced that even if the above impression were so, one would still have to have in mind that the eventual mortality of secondary operations for stones overlooked and left behind would have to be added to the primary mortality of cholecystectomies with a lower percentage of duct explorations if a fair comparison were to be made of the two types of operative procedure.

COMMON DUCT STONES

Common Ducts	Cases Explored		Stones Found		Total Cases
1910-26	96	15 %	52	8.4%	619
1927-28	91	32.7%	38	13.7%	278
1929-30	49	35.8%	22	16.1%	137
1930-31	61	42.5%	30	21 %	138
1931-32	45	38 %	22	19 %	118
1932-33	52	46 %	24	21.2%	113
1933-34	42	35 %	21	17.6%	119
1934-35	48	35 %	17	12 %	143
1935 to September, 1935	48	44 %	21	18.9%	112

As the result of this experience, we are convinced that it is the obligation of all surgeons who operate on patients for gallstones to make every reasonable effort to be certain that, in operations upon the gallbladder for gallstones, or cholecystitis (recall that stones were found in the bile ducts with no stones in the gallbladder in four per cent of the cases) stones are not left in the main bile channels. In order to do this, one must establish, we believe, wider criteria for opening and exploring the common duct than have been commonly employed by *many* surgeons in the past years. We believe that common and hepatic ducts should be explored in all jaundiced patients and in all patients in whom a reasonably recent history of jaundice is present, in all patients with a markedly thickened or contracted gallbladder since long-standing cholelithiasis and gallbladder infection make conditions so favorable for the production of duct stones and is so frequently associated with stones. We believe that the common and hepatic ducts should be opened and explored when the common duct is either thickened or dilated particularly when the gallbladder has not previously been removed. We believe that the common and hepatic ducts should be opened and explored when any suspicious lump suggesting stone can be felt on palpation of the ducts between the palpating thumb and finger.

We believe that the common and hepatic ducts should be opened and explored particularly in the presence of cholelithiasis or cholecystitis when the head of the pancreas is so thickened and indurated that stones at the ampulla of Vater within the thickened head of the pancreas could be overlooked. We believe that the common and hepatic ducts should be opened and explored when bile withdrawn into a hypodermic syringe, the needle of which has been passed into the duct, is not golden yellow in color and perfectly transparent and clear in character. While valuable information may be obtained by this latter procedure, we have not considered or recorded this measure as an exploration of the ducts.

Even in the presence of the above indications, we have found stones in only fifty per cent of the cases in which with these indications the ducts were explored. We believe, however, that stones exist in the main bile channels so often without definite evidences of their presence (jaundice, ability to palpate them, contracted gallbladder or dilated ducts) that many negative explorations must be made to accomplish a high percentage of complete removal of duct stones and a low percentage of a return of symptoms after the removal of the gallbladder for cholelithiasis or cholecystitis. (See table.)

CONCLUSIONS

A study of two hundred and twenty-one cases of common and hepatic duct stones is presented. This includes the sex incidence, the age incidence, the symptomatology incidence, the colic incidence, the chills and fever incidence, the jaundice incidence, the percentage in ninety-five cases of successful x-ray diagnoses and failure, the accuracy of duodenal drainage as a diagnostic measure in thirty-two cases, the end results in one hundred and forty-one cases followed for from one to ten years and the percentage of cases of common and hepatic duct stones in which stones were present and were not present in the gallbladder.

Figures are presented year by year showing our percentage of common and hepatic ducts explored and common and hepatic duct stones discovered up to this day.

Criteria are cited which, from our experience, justify exploration of the ducts for stones.

If one wishes to find and remove as many duct stones as possible, many ducts must be searched on suspicion and many negative searches must be anticipated.

Any argument that this teaching is dangerous in that it may cause additional mortality by prompting the inexperienced to open common

ducts is in our opinion fallacious. No one can justify the removal of a gallbladder with stones in it without adequate investigation for possible common and hepatic duct stones and with the proved high incidence of these stones, no one should undertake the surgery of cholelithiasis without the training and experience to investigate, adequately and with reasonable safety, the common and hepatic ducts.

DISCUSSION

DR. HOWARD M. CLUTE, Boston, Mass.: The frequency with which common and hepatic bile duct stones are found is certainly, as Dr. Lahey, Dr. Cheever and others have shown, related very definitely to the frequency with which we look for them.

It has always seemed a curious and anomalous situation, when operating on a gallbladder filled with stones, to find two or three stones in the common duct in spite of the fact that the duct appears normal in size and consistency and that there is no edema or thickening in the head of the pancreas. Very commonly these stones closely resemble those in the gallbladder.

I believe that certain of these common duct stones are pushed through from the gallbladder and cystic duct into the common duct in the course of the operation of cholecystectomy. The first step in cholecystectomy is to grasp the gallbladder with forceps and then proceed with a dissection of the cystic duct. These maneuvers forcibly compress the gallbladder and could easily force stones or detritus from the gallbladder or cystic duct into the common duct.

I have had, this year, two experiences confirming this. In the first, the common duct was opened before removing the gallbladder and two stones were removed from it. Following this the gallbladder was removed. A second examination of the common duct after the gallbladder was out revealed two more stones which were identical with those in the bladder, and which it was thought had been pushed into the duct during the dissection.

A similar situation arose in another case this year, in which detritus in large amounts, similar to that in the gallbladder, was discovered in a common duct which I had previously explored and found empty.

It would seem, therefore, that in the list of indications for exploration of the common duct, we certainly should include the presence in the gallbladder of small stones and detritus, which could readily be pushed through into the common duct in the process of cholecystectomy. It would also appear to be a good plan to clamp the cystic duct before exploring the common duct. By this measure we may avoid some of the postoperative common duct stone colics which we all have now and then after an apparently simple cholecystectomy.

DR. ARTHUR W. ALLEN, Boston, Mass.: *Mr. President and Gentlemen*—I think we all ought to be grateful to Dr. Lahey for his contributions that have increased our consciousness of common duct stone. There isn't the slightest question of a doubt that a great many of us have removed gallbladders, feeling that the common duct was probably clear, and not opening it because the indications for exploration of the common duct were not well organized in our minds at the time. There are all of fourteen good reasons why we should take the common duct into consideration when dealing with biliary calculi. I am not going into those in detail again at this time.

I am very much interested in Dr. Lahey's statistics on mortality of common duct exploration. In a little less than five years at the Massachusetts General Hospital, we have had twelve hundred and nine cases of biliary calculus operated upon. Three hundred and eighty-six of these have had their common duct explored—32 per cent.

There has been a total mortality in the twelve hundred and nine cases, of fifty-one, or 4.2 per cent. There has been a mortality in the common duct explorations of seventeen, or 4.4 per cent—an increase of only .2 per cent.

In the three hundred and eighty-six cases that have had the common duct explored, two hundred and twenty-seven have had the outlet dilated with the Bakes dilators. Some of them have not had very much dilatation, perhaps not more than Dr. Cheever would accomplish with his silk woven catheters which we used prior to the time we had these metal instruments, but occasionally the dilatation was carried as high as fourteen millimeters.

In the two hundred and twenty-seven cases that had the papilla dilated, there were nine deaths, and in the one hundred and fifty-nine cases in which the duct was explored and the papilla not dilated, there were eight deaths.

We have had no such serious sequelae following dilatation as Dr. Lahey pointed out. We have been on the lookout for serious complications because we thought they might occur, particularly reflux of duodenal contents, but as yet we have not had any such instance.

Showing the trend of the times and our becoming more common duct conscious, in 1931 there were only forty-five ducts explored in our hospital. There were eight deaths in the entire group operated on in that year, regardless of whether the ducts were explored. In 1934, ninety-two of the cases had the ducts explored and there were only seven deaths in approximately the same number of gallbladder cases.

Interestingly enough, and perhaps due to some selection on my part because I have been particularly interested in the subject, during this same period I have operated on one hundred and twenty-two cases of biliary calculus, exploring the ducts in sixty-six, or 54 per cent. In those sixty-six cases I found stones in the ducts in thirty-five and stricture of the outlet in seven.

DR. DAVID CHEEVER, Boston, Mass.: *Mr. Chairman*—I became "common duct conscious" a little earlier than Dr. Allen possibly because I arrived at general consciousness somewhat before Dr. Allen.

I read a paper on the subject of my personal experience in gallstones before the Massachusetts Medical Society last June. I was led, in preparation for that, to review my experience. I realized that I had been rather more apt than my colleagues, in the early days of the Brigham Hospital, at any rate, to explore the common duct.

As a matter of fact, as Dr. Allen knows and has noted, I began the purposeful dilatation of the common duct in the papilla of Vater in 1914, using olive pointed graduated woven French bougies. I determined at that time, by study in the anatomical department and by clinical experience, that the normal calibre of the papilla is about number ten French and one could dilate it apparently easily up to about sixteen French.

I have carried that out quite regularly ever since in cases where the common duct has been opened, not always dilating it to sixteen, not always, in fact, dilating it at all, but usually. I simply want to

record that. My observation was published first, I think, in 1929, which was a few months after, but without knowledge of, the communication from our friend, Bakes, so our work was quite independent. He used graduated metal sounds which have been described and I used the ordinary French olive tipped urethral bougie.

I also want to supplement Dr. Allen's feeling and the feeling that I am sure Dr. Lahey has, although he has very wisely pointed out its possible dangers, that this purposeful dilatation of the papilla of Vater is a very important adjunct in promoting the passage of any débris or small stone that may be in the common duct. I base that on the apparent fact, as shown by follow-up records at the Peter Bent Brigham Hospital, that the incidence of secondary stones in the duct has been comparatively small. I also want to place on record my testimony that I have not had in any single case any serious consequences from the dilatation of the papilla.

I do not find myself quite in agreement with Dr. Allen's paper as to the extreme dilatation which he has carried out with entire apparent impunity. I think he has shown that it is done apparently with impunity, yet I do not, myself, carry it out quite so far.

Dr. Birnie assumed the Chair.

CHAIRMAN BIRNIE: Is there any further discussion of this paper?

DR. LAHEY: I would not have you think for a moment that I think this dilatation of the sphincter of Oddi is not a good thing. I think it is a great advance, and I think Dr. Cheever and Dr. Allen are perfectly right.

The only thing is, here are these two fatalities that are terrible to face and one must, I think, approach this dilatation cautiously. If you know the dilators, they run up to pretty good sizes, eleven millimeters.

DR. ALLEN: The imported ones run to 14 millimeters; the ones made in this country run up to 10.

DR. LAHEY: The large ones are of pretty good size. It may be that these ducts were too widely dilated. Dr. Arthur Allen has dilated dogs with them.

DR. ALLEN: To full capacity.

DR. LAHEY: Without producing rupture of the ducts. Nevertheless, the existence of these two fatal cases must, I think, make everyone a little cautious.

Just one other thing—after all, we are of necessity a group of technicians and have to consider surgery somewhat from that point of view.

We have for a good many years employed what I think is a very valuable measure in all gallbladder surgery and particularly common duct surgery. We take great pains to expose the foramen of Winslow and to pack it with gauze before we open the common duct. Detritus and infected material from the common duct gravitates directly down into the kidney pouch and into the foramen of Winslow, and we feel that it at least produces conditions favorable for the production of subdiaphragmatic abscesses, which not uncommonly are a sequela of gallbladder operations.

PROSTIGMIN IN THE DIAGNOSIS OF MYASTHENIA GRAVIS*

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RÉSUMÉ OF THE LITERATURE

PROSTIGMIN†, which does not exist in nature, was first synthesized in the chemical laboratory by Aeschlimann and Reinert in 1931[1,2]. Its therapeutic action on the intestinal tract was investigated by Carmichael and others[3] in 1934. They reported that the drug produced active movements in the colon without a definite forward passage of the feces and suggested that it might be used in conjunction with pituitrin in the treatment of postoperative distention of the bowels. Nothing was said in Carmichael's report about the action of the drug on peripheral nerves or voluntary muscles.

In 1934, Mary B. Walker[15], working at St. Alfregés Hospital in London, had occasion to try physostigmine, the non-synthesized drug similar in its chemical formula to prostigmin, in the treatment of a case of myasthenia gravis. Physostigmine salicylate, by hypodermic injection, caused a striking, but temporary, effect upon the paralyzed muscles. When 1/60 grain was injected, for instance, an ophthalmoplegic patient was able in a few minutes to open her eyes widely. When the dose was increased to 1/45 grain, the patient had a sense of discomfort and the effects on the musculature were no greater than with smaller doses. Walker observed also that when 1/30 grain was given by mouth, the effect was slightly augmented.

Little attention, however, was paid to this account until the same author described, before a meeting of the Royal Society of Medicine of London, December 14, 1934[16], the effects of the synthetic product, prostigmin, on a patient with myasthenia gravis. With a dose of 1/25 grain of prostigmin a return of power to the paralyzed muscles was noted about five minutes after injection, an effect which lasted six or eight hours. In order to overcome the stimulating action of the drug on the bowels, 1/125 grain of atropine was injected at the same time. The investigation of prostigmin therapy was continued by Pritchard[12]. Seven patients were treated by him; all showed some improvement within five minutes after injection. The effects of the drug passed off in about eight hours. Myograms were taken of three patients, which showed a maintained tension of the muscles under prostigmin. Similar results were reported by Pritchard and Walker[13], and their work

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†Dimethyl-carbamic ester of 3-oxyphenyl-trimethyl-ammonium-methyl sulphate.

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was confirmed by McAlpine[11]. Hamill[7] and Hamill and Walker[8] suggested that prostigmin might be of use in conditions other than myasthenia gravis; they tried the drug in patients with bulbar palsy, amyotrophic lateral sclerosis, alcoholic neuritis and traumatic neuritis. Although some effect was noted in each of these patients, Hamill stated that "the results so far obtained are less dramatic than those in myasthenia gravis". Further application of the drug in the treatment of myasthenia gravis was made by Denny-Brown[4], who suggested that physostigmine and belladonna by mouth might be of value for long-continued therapy, when intradermal injections were not advisable. When this method of treatment, however, was used by us, the results were not so good as those reported by Denny-Brown.

In none of the above papers was any emphasis laid upon the diagnostic value of prostigmin. Many of the authors, however, noted the quick and dramatic response to the use of the drug and some authors, particularly Hamill, noted the slight response in diseases other than myasthenia gravis. It is in regard to the value of the drug as a diagnostic agent that attention is directed in the following communication.

CASE REPORTS

1. *The action of prostigmin on patients with myasthenia gravis.*

CASE 1. E. T. (M. G. H. No. 336151), a thirteen year old girl, first noticed ptosis of the right eyelid in September, 1933. A month later the left eye became involved, and gradually the patient developed complete ophthalmoplegia with bilateral weakness of the facial muscles. The patient was admitted to the Neurological Service on March 29, 1934, at which time she showed paralysis of the extra-ocular muscles, bilateral facial weakness, and tiring of the arms after rapid movement. Studies of the spinal fluid and blood were negative for signs of disease. A diagnosis of myasthenia gravis was made and ephedrin by mouth was advised. A year later, in spite of the use of ephedrin, her condition was practically unchanged. Her total score on the diagnostic schema was 55. (Fig. 1.) The patient was given subcutaneously 3 cc. of prostigmin with atropine 1/100 grain. In about fifteen minutes she complained of a sensation of heat behind the forehead and aching in the eyes; there was a warm feeling in the upper abdomen. A few minutes later the ophthalmoplegia began to disappear, and at the end of half an hour was completely gone. The effect lasted about two hours and then began to wane, and was gone completely at the end of four hours. There was no unpleasant reaction or sequelae. This drug was repeated on the same patient three times, with identical results in each case.

CASE 1. E. T. (M. G. H. No. 336151) April 4, 1935.

Time	Subjective	General	Local	Scale
0	0	0	0	0—No change
10 min.	2	2	3	1—Slight "
20 "	4	3	4	2—Moderate "
40 "	3	3	4	3—Marked "
1 hour	4	4	4	4—Complete "
2 hours	3	3	3	
3 "	2	2	2	
		Total	55	

FIG. 1 (Case 1).

CASE 2. M. K. (M. G. H. No. 344239), a fourteen year old girl, complained of fatigue on talking, slurred speech, and difficulty in swallowing, all gradually coming on during the three months before admission, April 5, 1935. A very slight facial weakness on both sides was observed and, after thirty seconds of conversation, slurred speech which became unintelligible after a minute. Swallowing was slow and awkward after one or two attempts. There was some weakness of both hand grasps on repeated use. Her total score was 49. The patient was given subcutaneously 3 cc. of prostigmin with atropine 1/100 grain. Fifteen minutes after injection she was able to read out loud for thirty minutes without fatigue. At the same time it was noted that swallowing and palate movement were normal and that there was no weakness in the use of the hands. The patient remained symptom-free for about two and a half hours; the symptoms then began to come back, and she showed no effect of the drug after four hours. The drug was used in this patient three times with similar good results. This patient was also given ephedrin and physostigmine by mouth without effect; digitalis by mouth in large amounts gave very slight improvement.

CASE 3. F. R. (M. G. H. No. 341290), a sixty-four year old male, entered the hospital on November 8, 1934 because of eighteen months of gradually progressive difficulty in speaking and swallowing. His speech was slurring, there was ptosis of the right eye, bilateral facial weakness, immobile palate, and awkward and slow swallowing. He improved after taking a course of ephedrin and glycine by mouth. Six months later, however, his symptoms were present, although not so disabling, and he was obviously still suffering from myasthenia. His total score by diagnostic test was 49. He was given prostigmin, 3 cc. with atropine, 1/100 grain subcutaneously. Just before the medicine was administered, on swallowing some barium before the fluoroscope, regurgitation was observed. Fifteen minutes after taking the drug he was able to talk normally, swallowing before the fluoroscope showed no obstruction, there was a marked improvement in the patient's ptosis, and the facial weakness disappeared. The effect lasted almost three hours and then disappeared. The effect was repeated on subsequent trial of the drug.

CASE 4. J. B. (M. G. H. No. 321437), a fifteen year old schoolboy, entered the hospital on May 20, 1932. He showed muscular weakness in many voluntary muscles, particularly in his legs, his hands, and in the muscles of mastication. He had difficulty in keeping his eyes open. There was also a right sixth nerve weakness with resultant diplopia and sluggish deep reflexes. Under ephedrin he showed some improvement. Readmitted to the hospital in 1933, his condition had progressed. His diagnostic test was 47. In April, 1935, he was given prostigmin. In about fifteen minutes his reflexes returned and the right sixth nerve paralysis disappeared. The effect wore off in about two hours. His gait, which was slouching and rather awkward before, was quite normal and strong while the drug was effective. This dose was repeated three times in this patient with similar effect.

CASE 5. M. L. (M. G. H. No. 348958), a forty-seven year old woman, entered the hospital, October 16, 1935, complaining of progressive difficulty in swallowing of eight months' duration. General lassitude and easy fatigability were noticed six months before entrance with some difficulty in swallowing for ten weeks. There was paralysis of the palate, with inability to swallow solid foods. Her speech was nasal in quality, her grips weak and walking was difficult. The diagnostic test gave a reading of 36. Under the effects of prostigmin, swallowing and talking were performed normally twenty minutes after the injection. The patient also improved under ephedrine.

2. *The action of prostigmin on patients with conditions other than myasthenia gravis.*

CASE 6. M. M. (M. G. H. No. 345299), a twenty-three year old male, came to the hospital on May 9, 1935, complaining of weakness in his arms of about six months' duration. His grip was weak and the calf muscles were hypertrophied. With 3 cc. of prostigmin and atropine 1/100 grain injected subcutaneously, no change in his condition was noted. His diagnostic test score was 2. The final diagnosis was *muscular dystrophy, hypertrophic type.*

CASE 7. W. H. (M. G. H. No. 346205), a man aged thirty-nine years, had been losing strength in his legs for four or five years. Weakness was also noted in his back muscles, with atrophy of both the back and legs. A biopsy examination of the muscles disclosed *progressive muscular dystrophy.* Prostigmin in the usual dose caused no effect.

CASE 8. F. P. (M. G. H. No. 346002), a twenty-two year old male, complained of progressive weakness of both legs over a period of six months. Although the muscles of the shoulder girdle and pelvis showed some atrophy, there was none in the legs. A biopsy examination showed muscle tissue characteristic of *progressive muscular dystrophy.* Three cc. of prostigmin were given without effect.

CASE 9. M. S. (M. G. H. No. 345928), a fifty-four year old woman, complained of the loss of the use of her legs over a period of two years. She also had difficulty in swallowing and talking. Her arms were atrophic and her legs spastic. The diagnosis was *amyotrophic lateral sclerosis.* Prostigmin gave a slight subjective sense of improvement, without objective signs. Her diagnostic test score was 7.

CASE 10. S. M. (M. G. H. No. 346578), a thirty-seven year old male, entered the hospital July 6, 1935 complaining of generalized weakness and difficulty in swallowing of six weeks' duration following an attack of sore throat. His gait was awkward and his grips weak. There was some discomfort in swallowing, considered as due to chronic, hypertrophied tonsils. Prostigmin was given with only slight effect, the diagnostic score being 6. The final diagnosis was generalized weakness following an acute upper respiratory infection.

CASE 11. I. K. (M. G. H. No. B. M. 18622, reported through the kindness of Dr. Walter Bauer), a fifty-two year old woman, entered the hospital May 20, 1935. She had weakness of swallowing, talking and moving the hands. Fibrillation of the muscles involved was marked. The diagnosis was *progressive bulbar palsy.* Prostigmin was given without effect. An autopsy confirmed the clinical diagnosis.

CASE 12. D. E. (M. G. H. No. P. H. 33287, reported through the courtesy of Dr. J. B. Ayer and Dr. J. C. White), a boy aged eighteen years, complained of ptosis of both eyes. This came on about six years before admission. The movements of the eye were also limited in all directions. Under prostigmin there was very slight improvement, the diagnostic test score being 4. The diagnosis was *progressive ophthalmoplegia of von Graefe.*

DIAGNOSTIC SCHEMA

The extra-ocular muscles and other muscles supplied by the cranial nerves are usually observed while standing behind the patient's head with the patient lying down. His gait and posture, however, are also observed from time to time during the test. Tests are done at stated intervals of time and the patient is asked to express his feelings each time an observation is made. The results are listed on a scale of 0 to 4. "Subjective" (fig. 1) relates to an increase in a general feeling of well-being. "General" indicates a decrease in paralysis of the larger muscle groups, such as the grip and ability to walk. "Local" reports the findings in smaller muscle groups that can be more accurately observed, such as the extra-ocular muscles, those of the face, and muscles used in talking or swallowing.

The "total" in cases of myasthenia ranged from 20 to 72; doubtful cases, from 10 to 20; negative reactions, from 0 to 10. Our positive myasthenia cases gave total scores of 55, 49, 49, 47 and 36. The negative cases tested gave totals of 2, 7, 6 and 4.

EARLY PHYSIOLOGICAL LITERATURE*

Rothberger[14] pointed out as early as 1901 that physostigmine antagonized curare in the peripheral nerve-muscle preparation. Gunn[6], in 1908, working on yohimbine poisoning, concluded that myasthenia gravis was a peripheral nervous, rather than a central, affection. Further light on the mechanism of the physostigmine-curare antagonism was cast by the work of the Lapicques[10], who observed that curare caused an augmentation in chronaxie while physostigmine, nicotine and veratrin diminished the chronaxie of skeletal muscle. In recent years there has been some discussion as to the validity of chronaxie determinations as a means of elucidating the problem of neuromuscular transmission, but these theoretical considerations do not affect the primary fact which the Lapicques were the first to emphasize, that curare diminished, and the physostigmine group of drugs increased, the excitability of muscular tissues, and that this was undoubtedly the basis of the antagonism of the two drugs.

Granted, then, that the state of the muscles in myasthenia gravis is akin to the state produced in them by curare, it is not unreasonable to suggest the use of physostigmine as a therapeutic measure. Edmunds and Roth[5] observed, moreover, that the effect of physostig-

*Contributed by Professor John F. Fulton.

mine on muscle appears to be separate from its action on the gut and various other organs innervated by the parasympathetic system, an observation confirmed and extended by Langley and Kato[9].

Nicotine and veratrin also augment the excitability of muscle, i.e., diminish the chronaxie, and they, too, tend to antagonize curare. Owing, however, to other toxic actions, especially of veratrin, it has not seemed advisable to suggest their use in myasthenia gravis.

DISCUSSION

The earlier work on the physostigmine-curare antagonism gave a suggestion that physostigmine or one of its derivatives might be of value in the treatment of myasthenia gravis, a disease characterized by weakness of muscles similar to the paralysis of curare poisoning. Such has proved, in part, to be the case. The rapid response to the derivatives, prostigmin, however, has furnished us with a new diagnostic test for myasthenia gravis, while its therapeutic action is still uncertain, except for temporary relief of symptoms. A diagnostic schema is helpful in recording the action of the drug. While the diagnostic test is of some use to medicine, it is to be hoped that prostigmin or another preparation may in the near future furnish us with a form of therapy capable of prolonged effect and thus be more suitable in the treatment of myasthenia gravis.

CONCLUSIONS

Prostigmin, a derivative of physostigmine, causes a marked, but temporary, remission of the muscular weakness seen in myasthenia gravis.

The effect is so marked that the drug is suggested as a diagnostic test for the disease.

Other diseases, either of nerves or muscles, respond only slightly to prostigmin.

Prostigmin is injected subcutaneously, with an appropriate dose of atropin to counteract any intestinal stimulation. Three cc. of prostigmin (Roche) and atropine, 1/100 grain, has proved to be satisfactory as a diagnostic test.

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A RECENT OUTBREAK OF FOOD POISONING IN SHOREHAM, VERMONT

BY R. F. DE WITT, M.D.*

OF a group of sixty men, women and children who ate home-made ice cream in December, 1933, forty-three were taken with an acute digestive upset. The refreshments consisted of vanilla ice cream with chocolate sauce, angel food cake, and coffee with cream. There were four gallons of ice cream, three of which were made by the same person, who stated that she had difficulty in freezing one gallon. The ingredients used were flour, eggs, whole cow's milk, evaporated milk, sugar, and vanilla. The resulting mixture was greyish in appearance and flat in taste. There was a question as to the cleanliness of the freezers.

At 11 P. M. lunch was served. Between 1 and 7 A. M. forty-three of the sixty persons were taken with acute symptoms which included, in most instances, nausea and vomiting, headache, muscular cramps and aches, weakness and marked prostration. The weakness, prostration, headache and muscular cramps persisted from ten to seventy hours from the time of onset. In the cases which were examined by a physician, temperature from 98.4 to 99.6 degrees F. and pulse from 72 to 96 were noted. No diplopia, nystagmus, photophobia, pharyngeal, or aural difficulties were apparent. Four of the forty-three victims had puffiness of the eyelids. One child of fourteen years, who ate a considerable amount, had nausea and vomiting and an irregular and thready pulse of 140, which lasted about twenty-four hours. Several individuals, who suffered milder attacks, had similar recurrences of their symptoms about twenty-four hours later, with no possibility of obtaining any of the above-mentioned food. Individuals, who felt general malaise and slight nausea about two hours after ingestion of the

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food, took large doses of saline or castor oil. Following this treatment their upsets were milder and recovery quicker than in those untreated.

In several instances diarrhea was noted at the onset, but in the majority there was constipation which lasted two to three days. In most cases, some degree of general malaise and gastric discomfort were present for about a week following the subsidence of acute symptoms.

Examination of ice cream, which was carried in a clean but not sterile container, was made four days following the party. Culture of the ice cream showed staphylococcus aureus, a streptococcus, bacillus coli, and an undetermined rod-shaped organism. Due to inadequate facilities an examination of the filtrate was not made.

A DETAILED CASE

The following is a detailed report of one case. The patient, aged forty-five, male, was seized with intestinal cramps and diarrhea four hours after the ingestion of the food; nausea and vomiting came on a few minutes later and continued for four and one-half hours at which time morphine and codeine were given. The patient was restless and confused, and vomited at short intervals during the next six and one-half hours. During this time he complained of a severe frontal headache and aches and pains in his muscles. These aches and pains lasted about eighteen hours. Prostration occurred about eight hours following the appearance of symptoms and lasted approximately thirty-six hours. Twelve hours after the onset of symptoms, the temperature was 98 degrees F., pulse 78 and respiration 17, with a maximum forty-eight hours later of 99-82-16. Eighteen hours after the onset, sodium amytal grs. 6, sodium bicarbonate gr. 15, sodium chloride gr. 15, sodium bromide gr. 15, were given per rectum in eight ounces of tap-water; this kept the patient quiet for about two hours. After the first twenty-four hours of the illness, a scarlatiniform rash appeared on the trunk and arms; this lasted about thirty hours, gradually fading away. Enemas and alcohol rubs had a sedative effect. General strength returned slowly the following week with no apparent complications or sequelae during a period of ten months.

SEVERAL SIMILAR OUTBREAKS RECENTLY REPORTED

Staphylococci were first reported as occurring in milk by Barber[2], who isolated both the white and yellow varieties; the white gave the investigator symptoms while the yellow did not.

Outbreaks of food poisoning ascribed to staphylococci following the ingestion of such foods as layer cake, cheese, devil's food cake, chocolate éclairs, wedding cake, cream puffs, chocolate cream pie, French vanilla ice cream and Christmas cake have been reported by Dack[3], Jordan[4, 5], McBurney[1], Nelson[6], and Arthur[7].

Gilbert, Coleman and Laviano[8], report B. cloacae, B. proteus and staphylococci as being the probable cause for gastrointestinal disturbances. In October, 1930, following an outbreak attributed to cream-filled pastries, from which staphylococci were isolated, symptoms were not produced by feeding filtrates to various laboratory animals, but upon feeding growths of a non-motile, gram negative, encapsulated bacillus, toxic symptoms were evident. Further study indicated that these organisms were of the cloacae-aerogenes group although they did not correspond exactly to any species for which a description could be found.

SUMMARY

Due to the short time between the ingestion of the food and the onset of symptoms, the probability of a chemical or a combined chemical and bacterial rather than bacterial origin appears logical. But, in view of the above reports of food poisoning with a staphylococcus or a member of the cloacae-aerogenes group as the apparent etiological factor, it seems probable, since the symptoms in the outbreak reported above correspond closely with other records, that the etiology in this instance might well be the same.

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VERMONT STATE MEDICAL SOCIETY

PRACTICAL LIMITATIONS OF VACCINE AND SERUM THERAPY*

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THE practicing physician must do something for his patient—anything that promises to be helpful. Perhaps the less clearly the measures are understood, the more alluring they are, especially if they are in the nature of a specific. Specificity, of course, is the underlying principle of vaccine therapy and that relationship is thus connoted whenever a vaccine is suggested, whether or not there is any real scientific basis for it. From this point of view, one must consider the practical value of vaccine therapy. Its limitations have been more sharply defined each year as medical science has been advanced by research in the laboratory and by clinical experience at the bedside.

One must understand clearly what one means by a vaccine. In the first place, it is an antigen. Now an antigen is a substance that, when introduced into the tissues, induces a reaction, in other words, varying degrees of injury, followed by recovery—a reparative process which becomes specific in its relation to the particular agent that incited the injury. In general, antigenic action has been limited to the protein substances but their action is now known to be modified by the presence of the carbohydrates. It is conceivable that a useful vaccine might be prepared from any microörganism that gives rise to an infectious disease but, up to the present time, the practical value of comparatively few has been convincingly demonstrated. In general, vaccines are used in the prevention and treatment of infection. Vaccine therapy differs fundamentally from serum therapy in that it induces an active immunity and a lasting one, whereas serum therapy provides only passive immunization which is quite evanescent. Thus, in general, vaccine therapy finds its sphere of greatest usefulness in the prevention of infection by developing an immunity before infection has taken place, whereas serum therapy is limited more and more in practice to the treatment of infection. Serum therapy, if effective, is immediately effective. Immunization with vaccines requires time for the active immunity to develop and thus varies greatly with the different vaccines. Although this, in general, is true, nevertheless, vaccines are useful under certain conditions and in certain types of infection which may be defined as the prolonged infections of low grade, in which the disease process is not developing an adequate immunity and requires the further stimulation that might be derived from judicious treatment with a potent vaccine.

If one accepts the broad point of view I have taken in defining a vaccine, it is obvious that toxins, as well as suspensions of the bacterial cells, should be included—although at the present time the term vaccine often connotes simply a suspension of bacterial cells: this usage disregards the origin of the term as applied to smallpox vaccine, which is not a bacterial suspension but a virus preparation. Moreover, smallpox vaccine is administered in the living state and owes its effectiveness to the fact that it is living and induces a modified form of the disease process from which is derived the immunity. This brings us to a fundamental differentiation in the action of these two types of vaccine—that derived from the bacterial incitants of infection as contrasted with that from the filtrable viruses.

Immunity to bacterial infection can be and is obtained by immunization with dead bacterial cells or their toxins, whereas it is extremely doubtful if an effective immunity against the virus diseases can be obtained without the introduction of the living virus and the development of some form of disease process in the tissues. There is another fundamental difference in the character of the immunity that is induced by these two agencies. Dead bacterial material, whether derived from the bacterial cells or the toxins, may induce an extremely high degree of immunity which subsides and becomes latent when immunization has stopped, just as it does after the recovery of a person from bacterial infection. In many of the infectious diseases, a second infection is rare; in a few it occurs not infrequently, for example, in pneumonia, as you all well know. After recovery from the virus diseases, a second infection is extremely rare. The immunity is lasting; practically permanent for the duration of life. Similarly, after the administration of a living virus in a vaccine, the immunity is likely to be lasting, with extremely rare exceptions—as for example, in the case of smallpox that develops in a person who has been vaccinated. The disease in such cases has been reported as modified and mild. The explanation that has been offered recently is extremely interesting, although further study is needed before one can venture to accept it, namely, that when these filtrable viruses enter the tissues as the inciting agent of an infectious disease or are injected

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as a vaccine, a harmless state of parasitism or symbiosis develops with recovery; and the virus which, in the tissues finds its natural habitat inside the cells, persists and continues living in the cells of its host indefinitely. Thus it is that individuals who have recovered from some of these virus diseases continue to have in their blood, years after recovery, specific substances that have a protective action on the virus when tested in the laboratory.

Further elucidation of the broad principles underlying the practical limitations of vaccine therapy would require all the time at my disposal and might serve no very useful purpose. Then, too, I fear I should become involved beyond my depth. Practical illustrations may serve much more effectively and to a better purpose, especially since they are doubtless of more interest to you as practicing physicians.

The list of bacterial vaccines that are, in varying degree, effective, is a long one; doubtless the list of those that are of little or no value is much longer. A vaccine may be potent and not useful. When a vaccine is potent and its specific relationship to an infectious process established, its sphere of usefulness is also very sharply defined clinically. Theory and practice invariably coincide.

Suspensions of typhoid, paratyphoid, dysentery, pertussis, and influenza bacilli, of cholera vibrio, and of some of the pathogenic cocci and higher bacteria have all been used in the prevention or treatment of infection. *Staphylococcus aureus* and some of the actinomyces have been used in the treatment of localized infections under certain conditions. The treatment of furunculosis with staphylococcus vaccine, *ad interim*, to prevent recurrence, might be considered rational vaccine therapy but staphylococcus vaccine is of no value and may be harmful in the acute stages of infection, whether localized or an invasive general pyemia. Thus this agent is limited to prevention as are practically all this group of vaccines.

Typhoid vaccine is perhaps better known and has been more widely used for a longer period than any of these bacterial vaccines. Its practical value, however, is definitely limited to prevention of the disease and, in conditions of frequent exposure, as in the army campaigns, vaccination must be repeated at short intervals in order to maintain the immunity in the active rather than the latent stage. The latent or dormant period of the typhoid immunity that follows inoculation after longer or shorter periods in different individuals possesses some but not always adequate protection against the development of infection after exposure. There is considerable discussion at the present time regarding the selection of strains of the typhoid bacillus with which to prepare the vaccines. Some of the old Rawlins strains have been considered lacking in antigenic potency but, after all is said and done, our experience regarding the practical value of typhoid vaccine is derived from the use of this strain during the World War and other campaigns in various parts of the world for more than twenty-five years. It is the opinion of the medical officers of our army that the campaign in Flanders would have been impracticable without typhoid vaccine. Although similar in many respects, paratyphoid vaccine does not appear to be quite so useful—not that it lacks potency, but the character of the disease and the effect of active immunization differ to such an extent that paratyphoid vaccine is not so generally combined with typhoid vaccine as it was a few years ago. Similarly, the administration of dysentery vaccines has been practically abandoned although bacillary dysentery is endemic in many districts.

Cholera is another enteric disease in which vaccines have been used extensively but only as a preventive measure to control the spread of epidemics, and thus it is of little or no interest to us here in this country at the present time.

During the influenza epidemics, various preparations of the influenza bacillus alone or in combination with other species of pathogenic bacteria were used quite extensively. In my experience and from a review of the work of other observers, I have been unable to ascertain that they have been in the slightest degree effective clinically. Preparations of the influenza bacillus and related species, as far as we have been able to determine in the laboratory, have an extremely limited potency so that, despite any specific relationship of these microörganisms, their value in the prevention or treatment of infection is negligible.

The terminal complication of influenza is pneumonia, and pneumonia, except in rare instances, does not yield to any form of preventive vaccine therapy. It was thought for a brief period that this might be due to failure to select the proper type of vaccine but it was soon learned that recovery from one type of pneumonia may be followed by a second attack of the same type so that protective inoculation with pneumococcus vaccine, for a brief moment advocated by some authorities as a public health measure, is not practical and has never been adopted.

Pertussis vaccine, like that of the influenza bacillus, from our studies in the laboratory, possesses extremely limited potency and, despite its specific relationship to whooping cough, is of very doubtful value in either the prevention or treatment of the disease. The prolonged course that whooping cough often follows suggests that a vaccine might be useful for treatment after infection had developed but its practical value clinically is far from sharply defined—extremely doubtful—but, lacking potency, it is a harmless agent. Most of the vaccines

now prepared contain a high concentration of pertussis bacilli, ten billion organisms per cubic centimeter. Lack of potency and failure to obtain clinical results have suggested the use of vaccines from freshly isolated cultures of this microörganism, as of others in the same category. This is not a practical laboratory procedure on account of the time required for safe preparation of the vaccine. Moreover, there are no proofs as yet that it is necessary.

In presenting these examples of vaccine therapy, I have tried to stress not only the conditions in which they are useful and how these vary with the different vaccines and diseases in which they are used, but also to illustrate how closely theory, as developed from laboratory research, coincides with practice, as revealed by clinical experience. I have accordingly selected examples concerning which we have considerable information—sufficient to define their practical limitations on the basis of sound reason; but there is also a long list of vaccines concerning the efficacy of which we really know little or nothing. Take, for example, the common cold. For the past fifteen or twenty years, various bacterial and other vaccines have been suggested but not one of them has as yet convincing support. The multiplicity of the vaccines or species selected bespeaks a lack of knowledge not only of their potency but of their specific relationship to the infectious process. The only basis for the selection of some of the bacterial species that have been used has been the fact that they were present and isolated. That they were the incitants of the common cold or that if a vaccine were prepared from them it would be potent, has never been determined. Moreover, theory and practice also coincide in these negative results—complete absence of a scientific basis and quite indeterminate clinical results from its administration. Now, if recent studies are confirmed, the common cold is due to a filtrable virus. These nondescript vaccines of the present day will therefore fall in the category of the gunshot prescriptions of our forebears.

In striking contrast to the common cold, the etiology of some allergic affections of the upper respiratory tract, such as hay fever or rose cold, can be determined and vaccines prepared from the toxic material; vaccine therapy is most effective as a preventive measure in such instances.

Lack of convincing clinical results often suggests the use of autogenous vaccines prepared from microörganisms isolated from the individual patient. These are not limited to the treatment of common colds and conditions of the upper respiratory tract but are extended to infection of any part of the body from which one can obtain bacteria—usually exposed parts, contaminated by species other than the incitant. The value of autogenous vaccines depends entirely upon their potency in the first instance and, in the second place, upon proofs that the particular species selected is the specific incitant of the process to be treated—data which are often lacking in the common practice of preparing and administering these autogenous vaccines. I have no quarrel with the use of autogenous vaccines when these conditions are fulfilled and the patient is not suffering seriously from an acute infection.

Preparations of the toxins of the diphtheria and tetanus bacilli and of the hemolytic streptococci are all potent vaccines and their etiological relationship to the disease process is generally very clearly established, but even these preparations are of limited practical value. No one presumes to advocate their use in the acute infectious processes. Here we have general acceptance of the sharply defined practical limitations of this type of vaccine therapy and it very strikingly illustrates the points of view regarding other forms of vaccine. When these preparations are so toxic that it is difficult to use them unless modified, treatment with formaldehyde when carefully adjusted destroys their toxicity without injuring materially their antigenic activity. These toxins can, therefore, be converted into toxoids and used effectively. Comparatively little has yet been done with tetanus toxoid but I believe it will have a very practical, although limited, sphere of usefulness. You are all familiar with the preventive immunization against diphtheria that is now so generally used. It was first modified by the addition of antitoxin; then by treatment with formalin; and very recently the formalin product has been adsorbed on alum or other substances and found to be far more effective when administered in this form. We have been interested particularly in the study of toxoid precipitated on calcium phosphate because it offers certain advantages over the alum and appears to be as effective, but we have not as yet distributed this preparation for general use. The precipitated toxoid can be given in somewhat larger quantities and in one dose. It is a more effective immunizing agent—doubtless on account of the slower absorption. There is no question but that the public health program of immunization against diphtheria has produced results in diminishing the morbidity and mortality of diphtheria. It does not mean, however, that diphtheria never develops in vaccinated persons. This, of course, is due to inadequate immunization. Individuals vary in their response and a few fail to develop the necessary immunity. The present procedures suffice for the great majority.

The hemolytic-streptococcus culture may be divided into two parts from the standpoint of vaccine therapy: the toxic filtrates, which are potent antigens, and the bacterial suspensions,

the action of which as a vaccine has not yet been determined. Vaccine therapy and serum therapy alike, as they relate to streptococcus infection, are complicated by the fact that the toxins and antitoxins vary according to the strain. It is necessary to use a corresponding vaccine for preventive inoculation or a corresponding serum for treatment after infection has developed. The strains bear no specific relationship to any of the characteristic disease processes such as scarlet fever or erysipelas. The different strains are found with about the same frequency in each of these diseases. There is no specific etiological relationship; hence there is no specific vaccine or serum therapy as yet developed. Preventive inoculation with the toxin is therefore limited for the present to those who are constantly exposed; it certainly is not practical for general use with the preparations available. To obtain a combination of toxins that will protect against all hemolytic streptococci is the difficult problem. The time required for immunity to develop is also a practical limitation in epidemics. The number and size of the doses have been repeatedly increased since the procedure was first recommended.

Vaccine therapy may be said to date from Jenner's work on smallpox, which belongs to quite another group of infectious diseases. The vaccine therapy of this group differs fundamentally from that of the bacterial infections. Smallpox, rabies, and epidemic poliomyelitis in man and distemper in the dog are incited by filtrable viruses. There is no convincing evidence that the agent of the disease smallpox and the agent of the vaccine are different species. By passage through the cow, the vaccine virus becomes so modified that it gives rise only to a modified infection as compared with the disease smallpox. From time immemorial, protection against smallpox has been dependent upon a "take." This is the result of the development of the living virus in the tissues.

Similarly, in rabies, the vaccine prepared from the cord of infected animals, dried or treated with various chemical reagents, is a modified form of the virus that gives rise to hydrophobia. Its practical value is to be attributed to the long period of incubation in this disease, which permits active immunization of the tissues with the vaccine before the disease has time to develop and thus is preventive in its action. If the administration is delayed, treatment with the vaccine would be considered dangerous were it not for the fact that rabies is invariably fatal. In other words, when this virus finds lodgment and develops to the extent of inducing the disease, the virus survives but not the host.

There is corresponding experience with immunization of the dog against distemper. These vaccines proved of little or no value until it was recognized that the living virus must be introduced. However, experience with new methods has established the fact that very slight but sufficient immunity may be induced in the tissues by the introduction of dead vaccine and that this must be given as a preliminary treatment to the inoculation with the living distemper virus in modified form. If the dog is a very valuable one, it seems wise to repeat the injection of the dead vaccine before giving the living virus. Moreover, to be certain of saving the dog, serum therapy is often recommended to control the disease process incited by the living vaccine if this should become alarming.

Attempts to develop a vaccine therapy to prevent, and thus control, epidemics of poliomyelitis have been unsuccessful. Research has now turned to preparations of the living virus in the hope of obtaining a modified living vaccine that might be safely given the human subject, and this has not yet been accomplished. These are concrete examples of the limitations of vaccine therapy in the virus diseases.

There is still another group of diseases incited by other species of microörganisms such as the *Plasmodia* or the *Trypanosomae,* for which we have as yet no vaccine therapy and comparatively little information concerning the problems involved.

Serum therapy is passive immunization in contrast to active immunization—vaccine therapy. Serum therapy is thus the transfer of the products of an active immunization to the infected individual. A horse is hyperimmunized, that is, receives a long and accumulative course of vaccine treatment to develop an active state of immunity. In some instances, this can be accomplished in two or three months; with other bacterial products it takes a year or two before the horse reaches a sufficient state of hyperimmunization. The horse is then bled and the serum or concentrated preparations of the globulins are used for the treatment of the homologous type of infection.

These sera may be divided into two classes: those that are predominantly or purely antitoxic in their action, such as the diphtheria, tetanus, and botulinus antitoxins, as contrasted with those that possess protective activity against, such incitants of infection as the meningococcus or pneumococcus. The sera obtained by immunization with the hemolytic streptococci may possess both types of activity. You are all quite familiar with the antitoxic action of sera in neutralizing the diphtheria, tetanus, and botulinus toxemias; but with the meningococcus, pneumococcus, and streptococcus, the disease is characterized by a bacterial invasion of the tissues that does not occur in diphtheria, tetanus, or botulism. The problems of serum therapy are therefore greatly complicated. It is not only necessary to neutralize the toxic products of the bacterial incitant of the infection, but the bacteria that have invaded the tissue must be destroyed also.

These different sera, irrespective of antitoxic or antibacterial activities, are effective in the treatment of infection after it has developed. They may be useful as a preventive measure for a brief period. Diphtheria antitoxin as it was formerly extensively given to children exposed to diphtheria is an example, and the administration of tetanus antitoxin following accidents is another. Passive immunization with antitoxin or serum has a very restricted usefulness.

You are familiar with the practical value of the antitoxic sera—their unquestioned potency and specificity in the treatment of the disease and thus also the remarkable clinical results you have obtained with them. Nevertheless, there are very definite practical limitations to their usefulness. Even with diphtheria antitoxin, reports have reached me of the failure of treatment to control the course of the disease. Different observers have attributed the failure of diphtheria antitoxin to differences in the character of the diphtheria bacilli which give rise to the outbreaks that fail to respond to treatment or to lack of potency in the antitoxins that were used. I personally have been interested in endeavoring to determine whether the rapidly fatal course of some cases of diphtheria might not be due to complicating infection of the necrotic lesions induced by the diphtheria bacillus in the upper respiratory tract. The work of Prudden in the early days of antitoxin treatment of this disease stresses the importance of the streptococcus as a contaminating agent. However, this point of view is speculative and lacks the necessary proofs.

With present methods of standardization in this country since federal control, diphtheria antitoxin has not lacked potency. No convincing proof has yet been obtained that the toxin produced by the different strains of the diphtheria bacillus differs in its neutralization by the standard antitoxin. On the contrary, I have examined carefully strains of diphtheria bacilli isolated from serious outbreaks—notably one that occurred in Berlin in 1927—and found that the toxins of these diphtheria bacilli were all neutralized by the standard diphtheria antitoxin.

For the present, therefore, one must attribute the failure of diphtheria antitoxin to delay in its administration or to inadequate dosage. This is a most important conclusion because it not only applies to serum therapy in diphtheria but to serum therapy in all the infectious diseases. Serum must be promptly administered to be effective.

This is particularly striking when one considers the treatment of tetanus with antitoxin. Early in the disease it is of value, but the course of the disease is so rapid and vital tissues become so early involved that serum therapy in this disease depends entirely upon the prompt administration of the serum in adequate doses.

For precisely the same reason, the practical value of treatment of another disease that involves the central nervous system, botulism, is rendered practically useless by the delay in securing and administering the serum. The poisoning is so acute that the central nervous system is immediately involved. It is usually impossible to obtain antitoxin of the proper type to administer in time to be of value. Patients, therefore, die or recover irrespective of serum therapy.

I must again stress these very striking examples of the practical limitations of serum therapy, dependent as they are upon prompt administration of these sera. In the treatment of epidemic meningitis, pneumonia, and scarlet fever and other streptococcus infections, this is especially important on account of the fact that with these infections the disease is complicated by the invasion of the tissues by the meningococci, pneumococci, and streptococci respectively; whereas diphtheria, tetanus, and botulism differ fundamentally in that they are toxemias without invasion.

The botulinus toxin, unlike the diphtheria toxin, is characterized by type specificity and it is necessary to use antitoxin of the corresponding type. Meningococci, pneumococci, and streptococci are also differentiated into types. It is therefore necessary to use either a polyvalent serum or one of limited valency corresponding to the type of the strain giving rise to the infection to be treated. By combining a few selected strains, serum of a potency approximating, equaling, or possibly exceeding that of monovalent sera can be prepared for the treatment of meningococcus meningitis. It would seem as though the relationship of the different types of meningococci differs in this respect from the pneumococci and streptococci. The results of serum therapy in meningococcus meningitis are very striking, but quite variable, depending upon the severity of the infection. The fulminating cases are difficult to treat promptly or effectively. Epidemics vary greatly in virulence and thus in their mortality. Hence, the results of the different series reported in the literature are not comparable. Dopter reports the lowest mortality—14.5 per cent—in treated cases. His results have not been obtained by others. Flexner reports 30.9 per cent deaths in his cases; 17.8 per cent failed to recover in our series.

There are practical difficulties in preparing sera of the requisite potency and breadth of valency with the different strains of the pneumococcus and streptococcus. In the treatment of pneumonia it is necessary to determine the type of serum to be used if satisfactory results are to be obtained. Moreover, in the treatment of pneumonia we find marked differences in the results obtained with serum therapy among the different types. For example, some

observers consider type I the only form of pneumonia in which treatment is of definite practical value. However, the sera of type II have been materially improved in potency and appear to be of value. Further study will be required to determine what types of pneumonia yield to serum treatment and to select groups of pneumococci that are more closely related one to the other in the hope of preparing sera of higher potency and broader valency. In any event, the serum therapy of pneumonia depends upon prompt diagnosis as to the type of infection. Fortunately, with the Neufeld's *Quellungsreaktion* this can be done without any delay. To a drop of the pneumonic sputum is added a drop of each of the different type sera. Immediately, under the microscope, is seen the swelling of the capsule of the pneumococcus that occurs in the corresponding type serum. When cases of type-I pneumonia are diagnosed and treated promptly and adequately, the mortality is reduced to approximately 10 per cent, whereas the mortality of cases treated late in the disease, or inadequately, approaches that of cases without serum therapy—namely, from 19 to 20 per cent in our series. These results correspond with those reported by Doctor Cole of the Rockefeller Institute.

I shall purposely avoid the controversial questions as to the treatment and dosage, but prompt administration—intravenous and intraspinous in meningitis, and intravenous in pneumonia—repeated at short intervals and continued until the results are manifest, practically everyone agrees, is the essential principle of serum therapy in these diseases.

The treatment of streptococcus infection is also subject to these cardinal principles. Progress in the development of serum therapy, as in preventive immunization, has been hampered by obsessions regarding the specificity of the different hemolytic streptococci with relation to a particular disease — scarlet fever, for example. The strains differ and, within certain limitations, can be classified; but our studies of fifteen hundred or more cultures from all sources have established the fact that the same strains are found in scarlet fever as in septic sore throat or erysipelas and they occur in about the same percentages in each disease; there is as yet no definition of a hemolytic streptococcus specific to scarlet fever, septic sore throat, erysipelas, or any other streptococcus infection.

From the standpoint of toxin production and the preparation of antitoxic or antibacterial sera, the strains of hemolytic streptococcus vary greatly. Comparatively few are of any practical value. Attempts are now being made to improve and broaden the therapeutic action of the sera. The difficulty has been that, in the attempt to broaden the valency, the potency has been sacrificed.

Serum therapy in streptococcus infection is further complicated by the fact that there are certain differences in the action of antitoxic and antibacterial sera not as yet fully understood. For example, we have recently learned that an antitoxic serum may have some protective or antibacterial action, providing it corresponds to the homologous type of streptococcus, but seemingly lacks this activity when tested with heterologous types. Nevertheless, it is inconceivable that the neutralization of the streptococcus toxin by potent antitoxin would not have a beneficial effect in aiding the protective mechanism of the tissues in a generalized infection.

In recent years I have followed this question of the practical value of antistreptococcus serum of high antitoxic potency in the treatment of generalized infections. Most of the cases have been treated late in the disease; many, when moribund. Nevertheless, there has been definite evidence of a beneficial effect although not determinative. Late in the course of the disease serum therapy does not alter the prognosis. Some of the patients have been treated early and the course of the disease prolonged; a few, a very few, appear to have recovered as a result of serum therapy. On the other hand, others have shown no change in the course of the disease. The results of serum therapy in scarlet fever, erysipelas, and septic sore throat, when it is started early in the disease, are often very striking and a crisis evidently induced. The clinical data are convincing. In scarlet fever there is only the question as to whether the disease is so mild as not to need serum therapy; but, mild scarlet fever may become a complicated generalized infection and the administration of serum is then too late to prove effective.

There is no question in my mind but that conflicting opinion regarding the practical value of antimeningococcus, antipneumococcus, and antistreptococcus sera in the treatment of infection during the past twenty years is to be attributed to the variation in the potency of the sera that have been available for treatment. During the War, many of them were practically worthless, but there has been a steady improvement so that the situation today is quite different. The progress that has been made through laboratory research in recent years toward a clearer understanding of the fundamental principles underlying vaccine and serum therapy in the different infectious diseases has defined more sharply their practical limitations, which in turn have been verified by the results of clinical experience.

DISCUSSION

DR. PHILIP HOWARD,* Detroit, Mich.: It is very worth while for us to hear such an authority as Dr. Wadsworth, for this is a question very close

*Not edited by Dr. Howard.

to us because when a new serum is prepared there is so much newspaper publicity about it that each of us has to decide what he is going to do about it, and whether he is going to use it.

I have had a good deal of experience in the use of pertussis vaccine. We have used the vaccine which has been publicized by Dr. Sauer, of Chicago, for the past three years. In the cases where we have used it, it is my personal opinion that we have not had more than two slight cases of whooping cough develop, and these were so mild that we had to resort to the use of the blood count and blood plates in order to be sure that we had an infection of whooping cough.

I would like to say a word about the use of the erysipelas serum. Before we had that, as described by Dr. Birkhaug, the mortality in the past ran around 60 per cent, but since we have used that serum the mortality has dropped to about 20 per cent.

About the use of convalescent serum, that is so limited that it is not a serum that can be used to wipe out an epidemic, but when available we have found that serum very useful.

In regard to the infantile paralysis I would like to say that our Board of Health agrees quite closely with what Dr. Wadsworth has said. They will not help us in using it and will not give their permission for us to use it in the vicinity of Detroit. Dr. Kolmer feels very strongly that his vaccine is a safe vaccine. We had a letter from him, within the past two weeks, in which he stated his vaccine had been used in 8000 patients, each receiving three injections, and he feels very definitely, that his vaccine is safe. Of course we agree with most public health authorities. It has been very pleasant to be here and listen to Dr. Wadsworth.

PRESIDENT MARSHALL: Perhaps Dr. Dalton will discuss this. It is a subject he is familiar with and interested in.

DR. DALTON: I am surely interested in this subject and also want to assure the members of the Society that we are very fortunate to have Dr. Wadsworth come here and read a paper on this subject. We have now pretty nearly the last word on the subject.

I would like to correct, if I may, the impression Dr. Howard seems to have about infantile paralysis being endemic in Vermont. To be sure, we do have a number of cases each summer, but I am sure, in studying reports from other states, that we have no more, per percentage of population, than many other states and less than some. The reason we are said to have more in Vermont is that we have been studying infantile paralysis intensively since 1914, and have not hesitated to tell about it, and it is probable that every diagnosed case is reported.

Returning to Dr. Wadsworth's paper, I am frequently impressed with the gullibility of the public, and many of the doctors, in regard to these vaccines and serums. Only within a few days, you probably have noticed, in one of the southern states, they have been using a serum which is supposed to be potent and specific for infantile paralysis, and the Public Health Department of that state has given its approval to the use of this, and there have been about 600 persons inoculated and pronounced secure against the disease. I expect this announcement has done a great deal of injury throughout the whole country, because people who are afraid of infantile paralysis feel, perhaps, that now the subject has been closed, and they may be following a false impression. Some of the doctors feel the same way in regard to the use of human immune serum. I appreciate the fact that when a doctor has a case of infantile paralysis he has to do something and he wants to do the thing which is for the best interest of the patient. When the doctors call me I tell them it is well to use the serum if they want to, but not to let the family think they now have a specific cure for infantile paralysis.

While serum may do some good, there are no statistics which show that it will prevent the paralytic stage from developing. In the Massachusetts series, it did appear that there were fewer paralysis cases which had the serum than in those which did not have the serum.

I hope that Dr. Wadsworth's report is printed and that every doctor will read it.

PRESIDENT MARSHALL: Dr. Wadsworth, will you close the discussion?

DR. WADSWORTH: There are some very interesting points in this discussion which I could not bring out in detail in my paper. As Doctor Dalton has mentioned the streptococci in poliomyelitis, I might add that I have talked with Doctor Rosenow of the Mayo Clinic, who has a broad point of view in regard to the biological adaptability of the streptococci, which we appreciate, but which, as applied to particular infectious processes, lacks definite proofs. For example, he has been unable to bring forward any convincing evidence that poliomyelitis is a form of streptococcus infection or that vaccination with the streptococcus is an effective preventive measure. On the contrary, his work in this field was not confirmed by Doctor Bull, then at the Rockefeller Institute. Doctor Gilbert in our laboratories immunized a monkey with the streptococcus which I received from Doctor Rosenow, but subsequently induced characteristic poliomyelitis in this animal following inoculation with the filtrable virus of the disease. We have been working intensively for ten years with the streptococci and it is extremely difficult to determine the biologic variation in the different strains. They vary in their toxigenic and antigenic action; comparatively few are of practical value in the production of potent antisera. It is largely owing to this fact that the commercial manufacturers of serum were handicapped by attempting to prepare sera with cultures lacking in the requisite potencies. It has been only since they have adopted new methods and special strains such as the Dochez N. Y. 5, which is now almost universally used, that the available sera have improved in quality. In the immunization of horses a year or two are required to obtain sera of high titer.

In regard to the serum from recovered cases of poliomyelitis, our experience has brought us to the conclusion that it is not of practical value. In 1931 we spent $100,000 to provide treatment for cases of poliomyelitis throughout the state. It is extremely difficult to diagnose the cases and treat them with the serum in time to have any recognizable effect on the course of the disease. Thus, it comes down to the original feeling that I had during the height of the epidemic and you as practicing physicians may agree with me, namely, that the important thing in the treatment of poliomyelitis is absolute quiet. Certainly I know of no preventive or other treatment that is effective.

For the past six years we have been studying the preparation of pertussis vaccine. In 1930 I discussed the problem with Doctor Gardner of Oxford, whose work stressed the selection of certain fresh strains. We have found quite marked differences in the strains but the selection and maintenance of those that are satisfactory antigens for the preparation of a vaccine have not yet been solved satisfactorily. It is important, however, to secure a strain that will retain its antigenic potency and maintain it under conditions that will preserve these properties.

PRESIDENT MARSHALL: We surely appreciate your coming here and giving us this excellent address.

We will now adjourn this session until two o'clock this afternoon, and the House of Delegates will meet at one o'clock in this hall.

Adjournment to 2 P.M.

MISCELLANY

VERMONT DEPARTMENT OF PUBLIC HEALTH

NOVEMBER, 1935

The following communicable diseases were reported to the office of the Department of Public Health during the month of November: chicken pox 336, diphtheria 4, measles 203, mumps 43, German measles 23, poliomyelitis 3, undulant fever 5, scarlet fever 39, typhoid fever 4, whooping cough 130 and tuberculosis 4.

The Laboratory of Hygiene made 1,706 examinations, the details of which are:

Examinations	for	diphtheria bacilli 133
"	"	Widal reaction of typhoid fever 36
"	"	undulant fever 63
"	"	gonococci in pus 141
"	"	tubercle bacilli 216
"	"	syphilis 531
"	of	water, chemical and bacteriological 109
"	"	water, bacteriological 248
"	"	milk, market 146
Examinations	of	milk, submitted for chemical only 6
"	"	milk, submitted for microscopical 1
"	"	foods 2
"	"	drugs 0
"	for	courts, autopsies 3
"	"	courts, miscellaneous 17
"		miscellaneous 53
Autopsies	to complete death returns 1	

The Director of the Division of Venereal Diseases reports twenty-six cases of gonorrhea and thirty-seven cases of syphilis made to this Division in November. Six hundred and fifty-eight Wassermann outfits and 312 slides for gonorrhea were distributed from this Division.

The After-Care Nurses of the Infantile Paralysis After-Care Division made 184 home visits, calling on 179 patients. One patient was admitted to the Audubon Hospital and one patient discharged from this hospital. Twenty-one pieces of apparatus were fitted, ten pieces of apparatus were repaired and forty-three orthopedic corrections made to shoes. The Vocational Worker of this Division reports sales made, amounting to $156.14.

Seven towns of the state were visited by the State Advisory Nurse of the Public Health Nursing Division, in the interest of the work of this Division. Part of the nurse's time this month was devoted to starting a project under WPA. One thousand and ninety-seven Notifications of Birth Registration and 700 pamphlets were mailed out in November.

THE BIRTH RATE THROUGHOUT THE WORLD

The gratifying rise in the birth rate which was recorded for the United States in 1934 was by no means world-wide. The long-time declining tendency in fact was still in evidence in 20 of the 34 countries whose 1934 birth rates have become available thus far. It is true that the drop in 1934 was less than 1 per cent in four countries, namely, The Netherlands, New Zealand, Italy, and Venezuela; and that in five instances—the Irish Free State, Norway, Sweden, Poland, and the Union of South Africa—the 1934 birth rate was identical with that for 1933. This may mark the end of the prolonged downward trend in natality in these countries.

Clearly, however, the declining birth rate still remains a problem in the social economy of 15 nations, where the decreases in 1934, as compared with 1933, ranged from 1.2 per cent in France and Switzerland, to 5.4 per cent in Spain, 5.6 per cent in Austria, and 6.3 per cent in Palestine.

Eight countries, in addition to the United States however, recorded rises in their birth rates in 1934, with the increases in most instances ranging between 2 and 3 per cent. By far the most noteworthy instance of an abrupt reversal of the long-time downward trend is Germany, where the astounding rise of 22.4 per cent was registered in a single year. Germany, in fact, is the only one of these 33 nations whose 1934 birth rate was actually higher than for any year of the 5-year period 1930 to 1934.

The birth rate for the United States for 1934 was 17.1 as compared with 16.6 in 1933, but these figures are below the rate of 18.9 for 1930.—*Statistical Bulletin*, Metropolitan Life Insurance Co., November, 1935.

MALARIA DEATHS

Officers of the Metropolitan Life Insurance Company are reported to have estimated that there are ninety thousand persons suffering with malaria in the United States.

Dr. L. L. Williams of the United States Public Health Service, is quoted in *Science* as believing that this estimate is too low. Malaria accounted for 4520 deaths in the United States in 1934, which is regarded as indicative of the figures cited.

MEDICAL PROGRESS

PROGRESS IN THE STUDY OF CARDIOVASCULAR DISEASE IN 1934

BY SYLVESTER McGINN, M.D.*

I. Introduction
II. Anatomy
III. Physiology
IV. Pathology
V. Etiology
  A. Congenital
  B. Rheumatic Heart Disease
  C. Subacute Bacterial Endocarditis
  D. Angina Pectoris
  E. Coronary Disease and Coronary Thrombosis
  F. Blood Pressure
  G. Cardiovascular Syphilis
  H. Thyroid Heart Disease
  I. Pulmonary Heart Disease
  J. Miscellaneous
VI. Symptoms and Signs
VII. X-Ray
VIII. Electrocardiography
IX. Pharmacology
X. Treatment
  A. Medical
  B. Surgical

I. INTRODUCTION

OUR knowledge of the cardiovascular system has been increased during the year 1934 by the contributions of a great many investigators. Their observations have done much to solve various problems associated with the circulation, have supplied valuable information to others engaged in research, and have afforded a better understanding to those confronted with complex cardiac situations in clinical practice. There have not been any observations of such great importance or sufficiently substantiated, however, to alter drastically our previous concepts or treatment of diseases of the heart.

Of outstanding importance in 1934 was the work initiated and carried on by a group of Boston physicians, which may ultimately provide the medical profession with a new method of treatment for patients with congestive heart failure and angina pectoris. Great and widespread interest is manifest in the progress being made on this problem of total ablation of the thyroid gland in heart disease.

The value of electrocardiography in the study of heart disease is well recognized. Several groups of investigators have been studying electrocardiograms more closely in the hope that they may give even more accurate information than has generally been expected of them.

There has been an increase in the mortality rate due to heart disease. *Cohn* and *Lingg* have reviewed the mortality statistics of the registration area of the United States to determine whether the death rate due to diseases of the heart was actually increasing. In the later decades a distinct, although not a great, rise has gradually become more evident in recent years. The apparent rise in the mortality rate of heart disease has largely depended upon the fall of the death rate of infectious diseases, not only of children but of all ages. At the Cook County Hospital at Chicago, *Flaxman* has estimated that 1.7 per cent of the patients admitted had organic heart disease. Because of the great frequency with which heart disease is encountered in the general practice of medicine, physicians everywhere have been attracted to and have developed a keen interest in the subject. To facilitate the study of the cardiovascular system, it is the purpose of this review to give a summary of the work concerning it done in 1934 by providing a bibliography and abstracts of contributions thought to be representative and of interest.

Two monographs of considerable value for special study have been published in 1934. *Cowdry* has edited a book of six hundred and seventeen pages on arteriosclerosis comprising twenty-one chapters written by twenty-three contributors. It is a useful reference book on this disease of the circulatory system. *Pal* has presented a monograph on the subject of vascular tension written with the viewpoint of correlating the physiologic mechanisms with the clinical picture. It is essentially a good review of the author's work and of the German and Austrian literature.

II. ANATOMY

Robb, Easby, and *Hiss* have performed further experiments showing that the heart consists of several muscle bundles arranged spirally, each with a specific blood supply, and from which they strengthened the impression that impulse conduction of the heart beats is in and runs parallel to the fibers of the ventricular muscle bands. Injury to a muscle band by compression, by ligation of its blood supply, or by transverse section, produces a result typical for that muscle bundle, namely, various electrocardiographic changes of the coronary type.

Gross has prepared specimens with anatomically open but functionally closed foramina ovale in such a manner that he can regulate the pressures in the right and left auricles. He has observed that an increase of pressure in the right auricle greater than that existing in the

*McGinn, Sylvester — Assistant in Medicine, Massachusetts General Hospital. For record and address of author see "This Week's Issue," page 1319.

left auricle results in the passage of fluid from the right to the left auricle; however, a reversal of this shunt is not possible. It is believed that this probably explains the occurrence of paradoxical embolism in cases having functionally closed foramina ovale although patent to the passage of a probe.

III. PHYSIOLOGY

Henderson and his associates believe that a third factor, in addition to the vasomotor nervous control of blood vessels and the pumping action of the heart, is necessary to the circulation. This is the force that sends the blood back to the heart through the venous system. They have found that a muscle in a state of tonus has an internal pressure of 50 to 70 mm. of water. If a muscle is in a state of tonus, it takes up through its elasticity some of the force of the incoming arterial blood. The pressure increases the venous outflow from the muscle and facilitates its return to the right heart. In flaccid muscles the force of the arterial pressure is lost and the venous return is impeded.

Robb and *Weiss* have found that the injection of sodium cyanide intravenously gives a reliable index of the velocity of blood flow in the pulmonary and peripheral venous circulations. No strict correlation was found between the clinical manifestations and the aspects of the circulation studied. As a rule, the slowing of the circulation time was proportionate to the severity of the congestive failure.

Determinations of the heart volume and stroke volume during rest in normal and decompensated individuals have been made by *Lysholm, Nylin,* and *Quarna.* The heart volume was calculated from x-ray measurements. In healthy individuals of different sizes under standard conditions the index of heart to stroke volume is nearly constant, and appears to be a measure of the functional condition of the heart during rest. In cardiac insufficiency the stroke volume falls below normal, whereas the heart volume increases.

Schneider and *Crampton* determined the output of the heart of several subjects in both the reclining and standing positions. There was an increase in the cardiac output after fifteen minutes when the subject changed from the standing to the reclining position. *Starr* et al have made estimations of cardiac output and determinations of metabolism, blood pressures and pulse rates on healthy individuals and on hospital patients for the purpose of seeking relationships by which the condition of the heart muscle might be ascertained. The relationship between heart work per beat and heart size holds more closely than any other studied. It was found to be abnormal almost without exception in cases that had once been decompensated. In patients with neurocirculatory asthenia the average cardiac output, stroke volume, and heart work per minute and per beat were far below normal.

Harrison and his associates have studied a group of patients with "evening dyspnea," which is described as the increased difficulty in breathing experienced by cardiac patients in the late afternoon and evening and is not to be confused with the paroxysmal type. It was found that the vital capacity was slightly lower and the oxygen consumption was ten per cent higher in the evening than it was in the morning. The respiratory rate was about fifteen per cent greater in the evening. As a result of animal experiments it was shown that the pulmonary afferent fibers of the vagus were very sensitive to pulmonary congestion and by reflex action stimulated the respiratory center. Because of increased bodily activity during the day it is thought that there is greater pulmonary congestion present at evening than in the morning and that this increase more readily irritates the nerve endings.

Gilligan and her associates found that the serum cholesterol value increased after total thyroidectomy and that the basal metabolic rate decreased. The most striking changes occurred by the end of the first postoperative month, although the serum cholesterol continued to rise gradually as hypothyroidism developed. The administration of thyroid resulted in an elevation of the metabolic rate and decrease of the serum cholesterol concentration.

Harrison has found a direct relationship between an increased venous pressure and the cerebrospinal fluid pressure in patients with congestive heart failure. As the patient improves and the venous pressure drops, the spinal fluid pressure also goes down. Removal of cerebrospinal fluid resulted in reducing the venous pressure in many of the cases, and in a majority of the patients there was a temporary decrease in dyspnea.

Interesting observations have been made by *Pickering* on the relationship between cerebrospinal fluid pressures and arterial hypertension. When the spinal fluid pressure was over 250 mm. water in hypertensive individuals, the patients were noted to be younger, the kidneys badly damaged, and the prognosis was very poor. Older hypertensive patients had lower spinal fluid pressures, the kidneys were less severely damaged, and the downhill course was less rapid. Albuminuric retinitis was thought due to neuroretinal edema, inasmuch as only the patients with a cerebrospinal pressure of over 250 mm. had these eyeground changes. There was no alteration in the pressure of the spinal fluid during headaches or acute attacks of coma. Some relationship is suggested between high diastolic pressures and high cerebrospinal pressures, although the latter seem unaffected by elevated systolic pressures.

IV. PATHOLOGY

Before making a comparative study of the diameters of arterioles of patients with and without hypertension, *Moritz* determined that there was no artefact due to the fixing process and none due to the physiological state of the vessel after death. The walls of the arterioles appeared to be definitely thicker in persons having persistent hypertension than in a control group without hypertension. However, some individuals in the hypertensive group did not have thickened arterioles. This is believed to be evidence supporting the contention that arterioles become thickened after long periods of high blood pressure and that this thickening does not by itself produce hypertension.

By feeding cholesterol to rabbits, *Leary* has been able to reproduce lesions very similar to those of human atherosclerosis. Evolution of the lesions through lipoidosis, lipoid cell formation, and fibrosis is much more rapid in animals than it is in man and consequently is more amenable to study. It is suggested that diets containing a high percentage of cholesterol may favor the atherosclerotic changes in the blood vessels. The paper contains excellent microphotographs illustrating the changes that have taken place in the vessels.

Schur has made an extensive review of the subject of adhesive pericarditis which has included a summary of the literature, the pathology and the pathologic physiology. From seventeen personal cases proved at autopsy, he has noted the clinical signs which form a rather complete symptomatology for this condition.

Levine reports finding at the autopsy of a ten months old infant a heart weighing 150 grams associated with diffuse thickening of the endocardium of the left ventricle, coaretation of the aorta, and stenosis of a portion of the left descending coronary artery.

An interesting case has been recorded by *Fischer* of a twelve and a half months old child whose heart showed rheumatic valvulitis at postmortem examination. The mother of the child suffered from polyarticular rheumatism at the third month of pregnancy and again at the fifth month postpartum. The case of a seven weeks old infant who died of bacterial endocarditis, the infectious process being superimposed on the mitral valve and in the absence of congenital lesions, has been reported by *Taussig*.

Calvin and *Nichamin* have reported two cases of spontaneous rupture of the thoracic aorta in children. Emphasis has been placed on the importance of rheumatic fever in such cases, inasmuch as this was the factor responsible in nearly one half of the forty-four reported cases of aneurysm of the thoracic aorta in persons under eighteen years of age.

V. ETIOLOGY

A. Congenital

Muir and *Brown* have studied forty cases having the physical signs of a patent interventricular septum. They encountered neither cases of heart block nor of permanent cyanosis, and believe that if either of these conditions is present, there must be an associated anomaly. The "maladie de Roger" has no characteristic x-ray picture.

B. Rheumatic Heart Disease

Rothschild and his associates feel that the majority of cases dying with heart failure in the first five decades and having a valvular defect are due to an active rheumatic infection rather than to the mechanical defect of the valve. Their conclusions follow the pathological study of one hundred and sixty-one cases dying with evidence of rheumatic heart disease. In the first decade active infection was present in 100 per cent of the cases, the percentage decreasing gradually to thirty-eight per cent in the fifth decade. Of the total number of cases fifty-five were quiescent, the youngest being found in the second decade.

Swift has directed attention to the varied symptoms indicating the chronic nature of rheumatic fever, such as prolonged low-grade fever, increased sedimentation rate and white count, and recurring arthritis. The greater susceptibility of individuals having had rheumatic fever to upper respiratory infections with consequent development of joint symptoms when ordinarily normal individuals overcome the infection without sequelae, is further evidence of the chronicity of the rheumatic infection.

Perry believes from his study of the sedimentation rates of children with rheumatic heart disease that the condition must be considered active if the sedimentation rate remains elevated and no other cause likely to maintain such an elevated rate is found.

Fraser has presented four cases of acute rheumatism in which endarteritis of the coronary vessels was present, apparently due to the rheumatic infection.

C. Subacute Bacterial Endocarditis

Although the protracted course of subacute bacterial endocarditis due to the streptococcus viridans is a common condition, an acute process with fatal termination due to the same organism is infrequent. *Held* and *Goldbloom* have reported four cases of acute and rapidly fatal streptococcus viridans endocarditis.

A review of three hundred and sixty-four cases of subacute bacterial endocarditis by *Weiss*, further confirms the general opinion that this disease most frequently follows infection of the upper respiratory tract.

D. Angina Pectoris

To produce attacks of angina pectoris and to evaluate the severity of the attacks, a tol-

erance test has been devised, which consists of determining the number of trips a patient can make over measured steps located in a chamber with controlled temperature. *Riseman* and *Stern* have reported their results in using this exercise test which they found very helpful in judging the status of angina pectoris patients.

Wayne and *Graybiel* found that there was an average reduction of twenty-five per cent in exercise tolerance in six patients with angina pectoris following a heavy meal. Distention of the stomach, however, by the introduction of air had no effect on the exercise tolerance. It was concluded that in angina of effort the exercise tolerance was diminished after food, because of the increased energy expenditure of the heart rather than because of gastric distention. External temperature changes had no effect on exercise tolerance of the six patients. A case is described of angina sine dolore where the symptoms were of substernal pressure rather than pain. Electrocardiographic studies showed that during these periods there was present a rapid ventricular action very closely resembling fibrillation.

White and *Sharber* have compared the frequency with which alcohol and tobacco were used by seven hundred and fifty patients with angina pectoris and by a control group of seven hundred and fifty individuals of the same sex and age incidence but without angina pectoris. An analysis of their observations shows that neither the use of nor the abstinence from alcohol or tobacco has any definite significance in the etiology of angina pectoris.

The occurrence of angina pectoris and intermittent claudication in patients with pernicious anemia has been described by *Pickering* and *Wayne*. Among twenty-five consecutive patients with anemia, the hemoglobin being twenty-five per cent or less, eight had precordial pain brought on by exercise and relieved by rest. Seven of the twenty-five anemic patients had pain in the legs brought on by walking and relieved by rest. After the anemia was cured, only one patient had pain in the legs and two complained of chest pain. It is believed that the leg pain is the result of the accumulation of metabolites in the tissues due to incomplete oxidation, and the anginal pain results from an insufficient oxygen supply to the cardiac muscle. The electrocardiograms of ten anemic patients showed only lengthening of the P-R interval in two cases which subsequently became normal when the anemia was corrected.

E. Coronary Disease and Coronory Thrombosis

Because of the frequency with which the diagnosis of coronary occlusion is made, *Barker, Wilson* and *Coller* cite four cases of upper abdominal disease closely simulating coronary thrombosis. Two cases of gallbladder disease were erroneously diagnosed coronary occlusion; a third case of perforated gastric ulcer required intensive study to establish the correct diagnosis; and in the fourth case both cholelithiasis and coronary disease were present.

In a statistical survey *Enklewitz* has found that coronary thrombosis occurred twice as frequently in diabetic as in nondiabetic patients. Of one hundred diabetic patients beyond forty years of age, thirty-four showed coronary thrombosis and forty-five coronary sclerosis. An opinion is expressed that both coronary thrombosis and diabetes in individuals over the age of forty years are manifestations of degenerative vascular disease. In a series of one hundred and fifty cases of coronary occlusion, *Blumer* found the incidence of the use of alcohol and tobacco almost exactly the same as in a control group of one hundred and fifty patients without coronary thrombosis.

F. Blood Pressure

Cushing has presented evidence suggesting that the source of eclampsia and essential hypertension may lie in the posterior lobe of the pituitary body. The activity of the posterior pituitary lobe is judged by the extent of basophilic cell invasion from the pars intermedia, and an excessive infiltration of these elements represents the histopathological basis of eclampsia and essential hypertension. Further study along these lines may provide valuable information regarding hypertensive states.

Ayman failed to find hypertension associated with any of two hundred and forty cases of active tuberculosis. Investigation of the past and family histories and the postmortem examinations of hypertensive patients showed that the tuberculous infection had been present at some time in life. Tuberculin studies with various dilutions showed reactions in ninety per cent of a group of patients with elevated blood pressures and in ninety-one per cent of a control group with normal blood pressures.

Levine made a gross and microscopical examination of twenty-seven hypertensive hearts. All of the hearts had minute myocardial scars, many of which contained varying amounts of elastic tissue. No correlation was found among age, sex, race, heart, weight, degree of blood pressure or the cause of death.

Adson and *Brown* sectioned the anterior spinal nerve roots on both sides from the sixth thoracic to the second lumbar in a twenty-nine year old woman with a blood pressure of 228 mm. systolic and 156 mm. diastolic. A report was made one month after operation, at which time the pressure was observed to be 168 mm. systolic and 128 mm. diastolic, when in the upright position. The effect of position was striking, the pressure always being lower in the upright

position than when recumbent. It is suggested that by lowering the blood pressure when the person is walking around, a certain strain is removed from the heart. The renal function apparently was unimpaired by the change in blood pressure.

G. Cardiovascular Syphilis

Burnett and *Rymer* found associated cardiovascular disease to be present clinically in 33.9 per cent of two hundred and fifteen patients with neurosyphilis. Electrocardiograms were abnormal or questionable in forty-seven per cent of one hundred and sixty-four patients so studied. The authors were impressed by the incidence of coronary changes found in their series.

Four cases of angina pectoris have been reported by *Van Muijden* and *Scherf,* the cause of which seemed to be a syphilitic mesaortitis in which the inflammation of the coronary ostia had produced a stricture. The prognosis of angina pectoris due to this cause is unfavorable.

Keefer and *Mallory* have reported twenty-two cases of aneurysms of the aorta complicated by pleural or pulmonary changes. These included atelectasis, bronchopneumonia, abscess, and bronchiectasis as the result of tracheal or bronchial compression of the lungs. Pulmonary tuberculosis occasionally accompanies aneurysm of the aorta.

H. Thyroid Heart Disease

Lahey and *Hurxthal* have reported an operative series of three hundred thyrocardiac patients defined as patients with toxic goiter in which the outstanding feature has been cardiac disability. The mortality after operation was 4.25 per cent. Seventy-one per cent of the patients with auricular fibrillation were restored to and maintained in normal rhythm, and compensation was restored in ninety-five per cent of the patients after hyperthyroidism was alleviated by a subtotal thyroidectomy. Preoperative therapy consisted in the administration of digitalis, Lugol's solution, and diuretics as necessary. Quinidine is used to restore normal rhythm but not until the fifth postoperative day.

Ernstene and *Mulvey* found that seven per cent of patients with hyperthyroidism had auricular fibrillation before operation and that sixteen per cent developed it after operation. Postoperative auricular fibrillation usually appeared within the first sixty hours after operation, without the occurrence of congestive heart failure, and normal rhythm was usually reestablished in forty-eight hours. The arrhythmia was more common in thyrotoxic patients having an adenomatous goiter than in those with hyperplastic goiter.

Lerman, Clark, and *Means* have added eighteen new patients to their original series of thirty myxedema patients in whom it was noted that the size of the heart diminished after starting thyroid medication. Of the eighteen new cases, fifteen had enlarged hearts, all of which, with the exception of one, decreased in the transverse diameter 1.3 to 4.6 cm. after treatment of the myxedema was instituted.

I. Pulmonary Heart Disease

Among anthracite coal miners *Dyson* found two hundred and thirteen cases of pneumoconiosis, of which number eighteen had complicating pulmonary heart disease or chronic cor pulmonale. The condition he points out is not uncommon and can be diagnosed in patients with pneumoconiosis by the presence of a large right ventricle and pulmonary conus, and right axis deviation by electrocardiogram.

Churchill has offered three explanations for the cause of death after pulmonary embolism. First, immediate death may follow complete obstruction of the pulmonary artery due to cerebral anemia and failure of the respiratory center; secondly, delayed death may be due to a condition resembling shock after partial obstruction of the pulmonary artery; and thirdly, delayed death may be due to right heart failure as the result of partial obstruction of the pulmonary artery. Comments were made on the Trendelenburg operation or the surgical procedure for the removal of clots from the pulmonary artery, on the basis of ten cases, none of which were successful.

Belt has observed that a high percentage of postoperative fatalities from pulmonary embolism shows evidence of minor degrees of cardiac incompetence.

J. Miscellaneous

A review of four hundred and ninety-six cases of myocarditis which developed in four thousand six hundred and seventy-one diphtheria patients has been made by *Hoyne* and *Welford.* The death rate of diphtheria myocarditis they found to be sixty-two per cent, death occurring usually in the first fourteen days of the disease. The mortality was highest in cases of nasal diphtheria, and of poor prognostic evidence were vomiting, abdominal pain, and a falling pulse rate and blood pressure. It was thought that dextrose solution given parenterally definitely helped some of the cases.

An etiological classification of neurocirculatory asthenia has been made by *Craig* and *White,* and an analysis has been made of one hundred cases of this disorder, fifty with organic heart disease and fifty without evidence of organic heart disease. Palpitation, respiratory discomfort, precordial aches, and exhaustion are considered to be the four cardinal symptoms of neurocirculatory asthenia, and when associated with sighing respiration and precordial tenderness the diagnosis is almost

certain. Radiation of the precordial discomfort into the left shoulder or arm is possible. The diagnosis of neurocirculatory asthenia must frequently be added to that of an organic cardiac condition where symptoms of the former are present.

In the opinion of *Warfield* no form of athletics other than college rowing injures a normal heart. He cites the studies of *Deutsch* and *Kauf* who found that occasionally a heart would become dilated after some form of sport. After rest the heart resumed normal size. It was believed that these hearts had previously suffered some muscle damage, probably from childhood infection. For this reason, it seems wise to be conservative in deciding when a child may resume activity after an infection. Slight systolic murmurs at the apex without cardiac enlargement he considers to be functional. Patients with valvular trouble are allowed freedom in activity within the limits of producing symptoms, providing there is no active infection present.

Purks has compared the causes of death after operation of sixty cases having organic heart disease with sixty postoperative fatalities having no heart disease. The first group of sixty deaths occurred in a series of four hundred and ninety-four operations on four hundred and fourteen cardiac patients and represents a mortality of 12.1 per cent and the second group occurred in sixteen hundred operations or 3.7 per cent. Congestive failure was found not to be an important cause of death, but the cardiac group was more susceptible to pulmonary infections and to fatal coronary occlusion.

VI. SYMPTOMS AND SIGNS

Friedlander and *Levine* have studied thirty-five patients, thirteen of which had paroxysmal or transient, and twenty-two, permanent, auricular fibrillation. Four cases of auricular flutter were also reviewed. In no case was there evidence of organic cardiac disease, and it was concluded that these arrhythmias were of functional origin. They represented six per cent of all of their cases of auricular fibrillation and twenty per cent of all those with auricular flutter. The majority of the patients were males, there being only three women in the series, and most of the patients were under fifty years of age. Quinidine sulphate is most successful in restoring normal rhythm, but daily doses of both digitalis and quinidine are helpful in diminishing the frequency of the attacks.

McGinn and *White* have reviewed one hundred and twenty-three cases of aortic stenosis proved at autopsy and one hundred and thirteen clinical cases, and have reported their observations. This valvular lesion was found almost as commonly as mitral stenosis, and the diagnosis could be made more frequently if it was considered. The majority of the cases had calcareous deposits in the aortic valves, both superimposed on old rheumatic infections and occurring singly. It appears justifiable to make the clinical diagnosis of aortic stenosis when a harsh systolic murmur is heard in the region of the second right interspace and in the absence of dilatation of the aorta. An aortic systolic thrill, diminished aortic second sound, or a plateau pulse, are helpful confirmatory findings but need not be present to make the diagnosis of aortic stenosis.

Following a clinical pathological study, *C. E. White* has concluded that arcus senilis does not occur in a sufficiently high percentage of older individuals to be considered a sign of senility, and because of the low percentage of occurrence in various forms of arteriosclerosis, it can hardly be indicative of that pathological condition.

Further studies in optical recording of heart sounds or phonocardiography have been carried on in South America. *Menéndez* and *Orias* made such records on one hundred healthy medical students and observed third heart sounds in forty-two of the tracings and evidence of vestigial third heart sounds in eighteen others. Auricular heart sounds were noted in fifteen cases; and in five, vestigial auricular heart sounds were found. Invariably the third heart sound occurs during the last moments of the ventricular inflow phase, and it is thought that they are due to vibrations in the ventricular wall set up by the in-rush of blood from the auricles.

Battro, Menéndez, and *Orias* studied twenty-two cases with definite audible gallop rhythms by recording the heart sounds simultaneously with the venous pulse. The timing of the sounds in the heart cycle was not constant, and varied especially with the heart rate. It was thought that gallop rhythm resulted from the pathological exaggeration of phenomena present but inaudible in normal individuals. Phonocardiography is in the process of development and may provide us with helpful clinical information that cannot be detected with the most careful use of the stethoscope.

Following an analysis of the physical signs present in twenty-three patients with bundle branch block, *Lewis* concluded that the nature of the signs did not permit their use in diagnosing the condition of bundle branch block. Records of heart sounds were made in all of the cases. Reduplications of the first sound, a presystolic gallop rhythm, and a palpable presystolic impulse were found frequently. Inasmuch as some of their patients did not have such signs and since they may occur in people without bundle branch block, their diagnostic value is small.

In these times of complicated laboratory procedures and specialized medical centers, *Har-*

rison has made an opportune comment emphasizing the importance of obtaining the patient's history in discussing functional tests of the heart. The best index of the capacity of the heart to do work is the patient's story as to the amount of activity required to bring on dyspnea. The most reliable index as to the condition of the coronary circulation is the amount of work that can be performed without producing angina pectoris. Other signs are helpful in judging whether the capacity of the heart for work is impaired, but of less importance than the subjective symptoms of the patient are the presence of gallop rhythm, an enlarged heart, electrocardiographic changes, and a diminishing vital capacity.

King, Hitzig, and *Fishberg* observed three cases of left recurrent laryngeal paralysis following failure of the left ventricle. Postmortem examination with careful dissection of the recurrent nerve was made in two cases. They concluded that the left recurrent laryngeal nerve runs through a triangle bounded by the arch of the aorta, the left pulmonary artery, and the ductus arteriosus, and that the nerve can be compressed by a dilated and distended pulmonary artery resulting from failure of the left ventricle.

VII. X-RAY

Ihre has reported the results obtained in using the Stumpf kymograph in examination of the heart. He found the method useful in that it gave a more detailed study of the movements of different parts of the organ. *Baird, Lingley,* and *Palmer* have reported the failure to obtain striking benefits in eight cases of severe essential hypertension treated by x-ray radiation of the pituitary and adrenal glands.

VIII. ELECTROCARDIOGRAPHY

Acute distention of the right heart chambers of dogs was produced by *Buchbinder* and *Katz* by means of clamping the pulmonary artery and injecting metallic mercury intravenously. Electrocardiograms taken failed to show right axis deviation. When mercury was employed, aberrations in the ventricular complexes were due to short circuits between the intracardiac metal and extracardiac electrodes. *Krumbhaar* reported electrocardiographic changes found after clamping the pulmonary artery of cats. Auriculoventricular block, ventricular fibrillation, and changes in the P and T waves were observed. It was thought that the changes were due to increased intraventricular pressure.

Katz, Hamburger, and *Schutz* induced a general anoxemia by rebreathing in seventeen normal subjects and in six patients with angina pectoris. Although electrocardiographic changes took place, only two subjects with angina pectoris complained of pain. The electrocardiographic changes consisted in diminution of the amplitude sometimes with inversion of the T waves and depression of the S-T segment. Because of the electrocardiographic changes in normal individuals as well as in patients with angina pectoris and the variability of the production of pain, induced anoxemia as a test for coronary disease is of questionable value.

McGinn and *White* have used the Lucas comparator to measure the durations of the QRS complexes of the electrocardiograms of one hundred and fifty normal and three hundred and fifty abnormal subjects. The average duration of the QRS complex in normal adults was 0.0777 seconds. Females and children under twelve years of age had average measurements slightly below 0.0777 seconds. In normal cases with duration times longer than 0.0900 seconds, particular variations in the QRS deflections, such as upright Q or S waves accounted for the prolongation. A note was made concerning inconsistencies in naming the QRS deflections with suggestions as to changes in nomenclature.

Edeiken and *Wolferth* call attention to the poor prognosis of M or W shaped complexes of an amplitude less than 5 mm. found in lead two. Their cases have been divided into two groups, the first of which contained twenty-one cases, and of this number fourteen are dead, six are incapacitated by severe myocardial disease, and one is untraced. Only two have lived more than three years after the M or W complex was observed. One tracing showed no other abnormal electrocardiographic finding. The second group contains twenty-five cases, of which number twenty had coronary occlusion, nine having died within two years. None of these electrocardiograms were normal in all other respects, although in eleven the changes were slight or inconclusive.

Korey and *Katz* injected ninety-five per cent alcohol into various areas of the ventricular myocardium of dogs. They concluded that the standard three leads cannot be used to differentiate injuries to the anterior and posterior walls of the ventricles, the right and left ventricles, and injuries to the basal and apical portion of the ventricles. No constant correlation could be made between the size of the injured area and the magnitude of the electrocardiographic changes.

Results of work done in further localizing areas of myocardial infarction in dogs' hearts by means of the electrocardiogram have been reported by *Wilson* and his associates. Ligation of the septal branch of the left coronary artery resulted in infarction of a large area of the septum. Electrocardiograms showed at first changes in the RS-T segment, later intraventricular or atrioventricular conduction disturbances, and all showed right bundle branch

block. They believe that the R deflection of the levocardiogram is not of septal origin and that most of the endocardial surface is active before the first deflection is written.

Additional electrocardiographic evidence of coronary infarction that may occur without changes in the T waves and that remains either definite or regressed has been offered by *Winternitz*. Necrosis of the anterior heart wall may be present when the R wave in lead one is small with deep S waves in leads two and three, or when the principal deflection of any lead is in the negative direction. Necrosis of both the anterior and posterior walls by two thromboses is suggested by the diminished amplitude of the main waves, although the smaller waves persist unchanged.

Barnes has reviewed eighty-four electrocardiograms of patients who had suffered acute myocardial infarction to determine the frequency of occurrence of the T_1 and T_3 changes described by *Parkinson* and *Bedford*, and the Q_1 and Q_3 changes described by *Wilson* and his associates. The former refers to the high or low origin of the RS-T segment in lead one, depending on whether there is anterior or posterior infarction. The opposite deviation of the RS-T segment is present in lead three. *Wilson's* classification is in reference to the presence or absence of Q waves in leads one and three, depending upon the position of the infarcted cardiac area. Although *Barnes* found the RS-T changes to be more typically developed, he feels most information can be obtained by considering both kinds of changes.

Durant has given the criteria to determine whether Q waves are abnormal. Excepting cases of right axis deviation, the Q wave in lead one is abnormal if it measures at least 1 mm. and is at least one-fifth as large as the largest R deflection of any lead. Curves of the Q_3 type are defined as those in which the Q wave in lead three is at least half as large as the largest QRS deflection. Because of the permanent character of these changes, they are thought to be valuable aids in recognizing coronary disease.

Shookhoff and *Douglas* have questioned the significance and evaluation of the so-called Q_3 wave of the electrocardiogram as commonly interpreted. They found that in normal ventriculograms the Q waves of all leads corresponded in time, but that in the tracings with large Q_3 waves they did not correspond in the timing of the ventricular deflections. In fifty cases of this latter type the Q_3 wave was found in most instances to correspond either entirely or in part with the R waves of leads one and two. For this reason, it is believed that the presence of a deep Q wave in lead three does not justify the assumption that a particular myocardial area is the site of disease and that it necessarily indicates coronary disease. They consider factors that change the relative position of the ventricular musculature, as by rotation of the heart by a high diaphragm, the most important cause of the "Q_3" wave.

In twenty cases that had come to necropsy after an acute myocardial infarction, *Barnes* found that fairly typical Q_1 and Q_3 changes corresponded respectively with anterior and posterior infarcted portions of the left ventricle and associated interventricular septum. However, not all acute infarctions of the left ventricle were followed by characteristic Q patterns.

Alterations in the T waves and in the S-T segments of the electrocardiograms of three patients with acute rheumatic fever have been observed by *Easby* and *Roesler*. Inversion of the T waves as seen in coronary disease and high or low origins of the S-T segment, both of which findings varied with the course of the disease, were noted. The literature has been extensively reviewed and they have found anatomical studies supporting the suggestion that such electrocardiographic changes are due to myocardial variations consequent to acute infection of the coronary circulation.

Bayley found that seventy of one hundred and seventy-three cases of bundle branch block had the less common type or right bundle branch block. He believes that right bundle branch block is more common than is usually thought and that bundle branch block is more frequently associated with arteriosclerotic heart disease than any other disease.

White has presented electrocardiograms of a patient having a recent coronary thrombosis superimposed on previous coronary disease, as indicated by left bundle branch block. After the more recent coronary occlusion, the T wave in lead three became inverted. Postmortem examination confirmed the suspected changes in the coronary vessels.

Barnes has found in a case of acute coronary occlusion with pericarditis that the RS-T segment is upright in all leads and so varies from uncomplicated cases. This difference should suggest pericardial involvement.

Lead four is thought by *Battro* and *Del Rio* to be helpful in establishing the diagnosis of angina pectoris. In four out of twenty cases of angina pectoris, lead four showed evidence of myocardial infarction, while the three conventional leads were practically normal. *Wood* and *Wolferth* have directed attention to the presence of large T waves in the precordial leads, as the result of observations on seven cases having the symptoms of coronary occlusion. These large T waves are obtained from only a small area of the precordium and disappear at a later date. They suggest that very large upright T waves indicate a lesion in the anterior portion of the left ventricle and very deeply inverted T waves in the precordial leads signify a lesion in the posterior surface of the left ventricle.

IX. PHARMACOLOGY

Scupham has found theobromine sodium acetate useful in the treatment of some early cases of thrombo-angiitis obliterans and intermittent claudication.

Van Liere and his associates produced cardiac dilatation in twenty-three dogs by diminishing their oxygen supply. The dilatation decreased after digitalis was given, and when the dogs were again subjected to atmosphere deficient in oxygen, the hearts failed to dilate as much as prior to the administration of digitalis. It was felt that the drug acted directly on the myocardium and increased the tone of the muscle.

König has attempted to prevent postoperative thrombosis and embolism by the administration of synephrin tartrate, a compound similar to and one-fiftieth as strong as epinephrin. The dosage is twenty drops by mouth or 1 cc. hypodermically three times a day for seven days. The patient also is given short inhalations of carbon dioxide every hour for from four to six days. Comparative observations on four thousand five hundred cases showed satisfactory results. The incidence of postoperative thrombosis and embolism was reduced from 3.8 per cent to 1.04 per cent, and the pulmonary complications were reduced from 9.4 per cent to 3.4 per cent.

X. TREATMENT

A. Medical

Barach and *Levy* have again emphasized the beneficial effect of supplying oxygen to patients suffering from acute coronary occlusion. They used most frequently a concentration of fifty per cent oxygen. In the discussion of their paper, several points of interest were brought out, namely, that with a nasal catheter a concentration of forty-two per cent oxygen can be maintained in the inspired air; sometimes a concentration of oxygen as high as ninety-five per cent is necessary to relieve symptoms; and occasionally the administration of oxygen succeeds in relieving the pain of acute coronary thrombosis when morphine has failed.

Marked relief of symptoms has been observed by *Sutton* in eleven cases of rheumatic pericarditis with effusion in which a therapeutic pericardial paracentesis had been done. From two cases of pericardial effusion that came to necropsy, it was learned that the distended pericardium almost reaches the posterior chest wall. This would seem to justify a posterior approach which can be done without penetrating the lungs.

Gilchrist increased the ventricular rate by administering ephedrine in four of six cases with complete heart block. The normal dose was one-half grain every eight hours, and it has been given for as long as two and a half years without harmful effect. He felt that barium chloride did not prevent Stokes-Adams seizures.

Evans and *Hoyle* have closely observed one hundred and twenty-two patients with angina pectoris to discover which of the many drugs they used was most efficacious in relieving or preventing the pain. Tablets of glyceryl trinitrate dissolved on the tongue were the most successful. When used before expected attacks it was frequently found to prevent them.

B. Surgical.

The superior and inferior thyroid arteries have been divided and ligated by *Lyon* and *Horgan* with beneficial results. By this procedure they were able to lower the basal metabolic rate, without producing myxedema, and so diminish the demands on the circulation.

Blumgart and *Davis* have described the procedure of completely removing the normal thyroid gland in the treatment of chronic heart disease. A hypothyroid state is induced which can be controlled by thyroid medication, so that the patients may be comfortable and still benefit by the reduction in cardiac work. Much relief has been given patients under the conditions of reduced metabolism, the symptoms of which are insignificant in comparison with the benefits derived.

Weinstein and his associates have concluded from their observations of nineteen patients whose chest pain had been relieved immediately after total thyroidectomy that this relief was due to interruption of afferent impulses from the heart. This relief was transient and not until the basal metabolic rate had been lowered was the chest pain permanently affected. The use of local anesthesia was thought unimportant, inasmuch as the immediate relief was also observed after the use of nitrous oxide anesthesia.

The group associated with *Blumgart*, interested in totally removing the thyroid gland in cases of congestive heart failure and angina pectoris, has presented its criteria in selecting cases for the operation. Both the preoperative and postoperative treatment of the patients have been outlined. The results have been encouraging thus far, but the final appraisal of this therapeutic procedure awaits the observation of a larger group of patients over a longer period of time.

DeCourcy, DeCourcy, and *Thuss* believe that a relationship exists between hypertension and hypersuprarenalism. They liken overactivity of the suprarenal glands to overactivity of the thyroid gland in hyperthyroidism. In cases of hypertension, they have been removing about two-thirds of each suprarenal gland in a two-stage operation. The beneficial effect on the hypertension is such that they advise this operation in selected cases.

Blalock **has reported successfully suturing a wound produced by an icepick in the intrapericardial portion of the ascending aorta.**

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THE INFLUENZA MENACE

Science reports that there is a possibility of an influenza epidemic in the United States this winter which is founded on the information received by the United States Public Health Service, that there are about five thousand cases of this disease in Honolulu. This epidemic started early in November.

The last big influenza epidemic, that of 1932, is reported to have started in Hawaii. It invaded the United States with a record of ninety thousand cases.

THE COMMUNITY FUND CAMPAIGN

The forthcoming Community Fund Campaign, serving one hundred hospitals, health and social agencies in the membership of the Community Federation of Boston, is receiving generous support from the physicians of Greater Boston. The goal set for the 1936 Campaign is $3,750,000.

"This amount will not fully meet the needs of the welfare agencies which are members of the Community Federation," says Ripley L. Dana, general chairman of the Campaign, "and these agencies will have to practise economies which to some extent will hamper them.

"But it seems more business-like to fix the goal at a figure which can be reached, even though it is less than the agencies require, than to fix a goal at a figure which will meet the requirements of the agencies, but which, at the moment and under present conditions, seems beyond the capacity of the community to provide.

"I believe that $3,750,000 can be raised. It must be raised. I hope this amount will be largely oversubscribed."

The dates set for the 1936 Community Fund Campaign are January 26 to February 10. Dr. John F. Monks is Group Chairman, and Dr. George C. Shattuck, Vice-Chairman, of the medical group.

DR. M. E. BINET WILL VISIT THE UNITED STATES

Dr. Binet, Vice-President of the Medical Society of Vichy (France), will visit the United States. The purpose of his visit is to extend an invitation to several American physicians to attend the International Congress of Hepatic Deficiency, which will be held in Vichy in 1937, presided over by Professor Maurice Loeper, Professor of Clinical Medicine at the Faculty of Paris.

TUBERCULOSIS IN BROOKLINE

As part of the Seal Sale Campaign the Brookline Anti-Tuberculosis Society has made public, through the Health Bulletin of the Board of Health, the following statistics:

"40 deaths, 1897, population 17,000; 8 deaths, 1934, population 50,000; 253 possible cases, 1935, to be watched and prevented; exposure to 80 children who have gone to summer camps annually for health and happiness; The Anti-Tuberculosis Society to help guard your health; planned action to combat the disease; . . . "

Case Records

ANTE MORTEM AND POST MORTEM

AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

AT THE

MASSACHUSETTS GENERAL HOSPITAL

Founded by RICHARD C. CABOT, M.D.
TRACY B. MALLORY, M.D., *Editor*

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CASE RECORDS

of the

MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 21521

PRESENTATION OF CASE

First Admission. A sixty-one year old white American artist was admitted complaining of pain in the right knee following an injury three days previously.

He had "heart trouble" eleven years before entry attributed by his physician to medication received for an attack of influenza which he suffered at that time. He had a left inguinal hernia for fourteen years. He had a "bad attack" of pleurisy at the age of fourteen. Two and a half years prior to entry he had an attack of sharp pain in the penis followed by hematuria. There had been no similar difficulty since.

His father died at seventy-four of cardiac failure; the mother died at eighty-seven with jaundice. One sister had heart trouble.

Physical examination showed a well-developed and nourished man. The chest was emphysematous. There was an occasional squeak audible bilaterally. The heart was not enlarged; the sounds were regular and of fair quality. The blood pressure was 140/80. There were bilateral inguinal herniae, the right being larger than the left. There was tenderness and swelling about the internal condyle of the right knee.

The temperature, pulse and respirations were normal.

He improved with physiotherapy and massage and was discharged on the fifth day.

Second Admission, two years later for repair of the left inguinal hernia.

Third Admission, four months later.

He had been well until twelve days before entry, when while walking up a hill he suddenly developed a sensation of constriction about the thorax at the level of the heart. There was no radiation. He continued to walk, became dyspneic, and developed tingling sensations in both arms and forearms. This persisted for twenty minutes and then subsided spontaneously. Three days later he was seized with a similar attack while sleeping. This was more severe and the tingling sensation was more marked in the left arm and hand. His physician gave him two pearls of amyl nitrite which afforded him considerable relief. He remained in bed for seven days but then arose for an anniversary dinner. At the table, while eating, another attack occurred which continued for four hours and was finally relieved by two hypodermics and six pearls of amyl nitrite. During the attack there was marked fear of death. He had no attacks after this but entered the hospital because of fear of recurrence. His weight which had been 170 pounds seven years before was now 140. There had been no dietary restrictions.

Physical examination showed slight puffiness of the lower lids. The sclerae were injected. There were leukoplakic spots on the tongue. There was a fatty tumor in the left posterior part of the neck. The fundi were negative. The apex impulse was neither seen nor felt. The left border of cardiac dullness was 10 centimeters from the midsternal line, 1.5 centimeters beyond the midclavicular line. The sounds were regular but distant. There was a blowing systolic murmur replacing the first sound at the apex. The second sound was sharp. A_2 was greater than P_2. The blood pressure was 140/85. The radials were thickened but compressible. A few inspiratory crackles were audible at the bases but disappeared quickly. The abdomen was protuberant. The hernia scar was well healed. The knee jerks were slightly exaggerated.

The temperature, pulse and respirations were normal.

Examination of the urine showed a specific gravity of 1.011 to 1.013. The sediment contained 15 to 25 white blood cells. The blood showed a red cell count of 5,000,000, with a hemoglobin of 80 per cent. The white cell count was 9,000, 67 per cent polymorphonuclears. A Hinton test was negative. An electrocardiogram showed a deeply inverted T_2 and T_3. P_1 and P_2 were notched. P_3 was inverted.

The x-ray showed no significant change from that previously taken. The transverse diameter of the heart was 14.8 centimeters, that of the chest being 28.7 centimeters.

On the fourth morning directly following breakfast he had an attack similar to the others, with a sensation of congestion in the left arm and in the left posterior part of the neck. This responded quickly following the administration of one-hundredth of a grain of nitroglycerine. He was discharged on the twenty-third day.

Fourth Admission, fourteen months later.

The patient had no further attacks of chest discomfort. He remained well until six weeks before reëntry, when he became constipated and noticed that his stools were thinner and contained material resembling "shredded tobacco". There were no bloody or tarry stools. He began taking a laxative daily. A short time later he developed dull aching pain across the upper abdomen which occurred directly after

meals and lasted for about an hour. It sometimes recurred during the night but for the most part returned only two or three times a week. There was associated gaseous eructation. The pain was not definitely localized and was not very severe. Occasionally it kept him awake and the fear of initiating it prevented him from eating a regular diet. Gradually he developed a sensation of fullness in the epigastrium after meals and thought food did not pass. After five or ten minutes this was relieved spontaneously. He frequently avoided this sensation by drinking hot broth before meals. There was no nausea or vomiting. His weight decreased about ten pounds during this illness.

Physical examination showed that he had aged considerably and was poorly nourished. The skin was loose and flabby. The abdomen was scaphoid. The heart was slightly enlarged to the left but there were no other changes. The lungs were clear. The abdomen was negative.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red cell count of 4,700,000, with a hemoglobin of 75 per cent. The white cell count was 13,000, 73 per cent polymorphonuclears. Examinations of many stool specimens were negative for blood. An electrocardiogram showed a split P_2. T_2 and T_3 were inverted. There was slight widening of Q-R-S, a rather low voltage and a slight elevation of S-T_2 and S-T_3.

X-ray showed a slight delay in the passage of barium through the lower end of the esophagus. There was no dilatation of the esophagus except when the patient drank barium rapidly. The fundus of the stomach protruded through the diaphragm at the esophageal hiatus. There was a diverticulum of the esophagus just below the aortic arch and a definite filling defect and constriction of the lower end of the esophagus due to a lesion 4 centimeters in length which apparently extended downward and involved the fundus of the stomach. The remainder of the stomach, pylorus and duodenum was negative. Three days later another x-ray showed dilatation of the lower third of the esophagus which included the diverticulum. The relief was irregular and there were bandlike areas of decreased density instead of the normal rugae. The entire area was soft and pliable except for the epicardia, which appeared to be rigid. There was a constant fleck about 3 millimeters in diameter in this region.

On the fourth day an esophagoscopy was done which revealed a hemorrhagic surface 11.5 centimeters from the front of the teeth. This bled easily when rubbed with a sponge. A specimen was removed for examination. During the second week the patient received repeated heavy doses of x-ray to the chest. He had little reaction to the irradiation but had considerable symptomatic improvement. The discomfort was relieved and he began to eat a full diet. He was discharged one month after entry.

Fifth Admission, six weeks later.

Since his last admission he felt very well, gained weight and continued to eat a full diet with no discomfort. Two days before entry he again developed a sensation of substernal discomfort while eating. Food appeared to "stick" for ten minutes. He retched considerably with no relief but finally took one-hundredth of a grain of nitroglycerin which gave complete relief.

Physical examination showed a partial compensation of his previous weight loss. The heart and lungs were unchanged. The liver edge descended about 3 centimeters beneath the costal margin with respiration. It was slightly tender but not nodular.

He was given another series of x-ray treatments and discharged without symptoms in three days.

Sixth Admission, ten weeks later.

He remained quite well for about two weeks after his discharge but then began to vomit soft foods. Emesis became more frequent and for two days prior to reëntry he was unable to retain anything. The vomitus contained food, mucus and a little yellow bitter material. There was rapid loss of weight and strength and the sensation of blocking was now felt higher up behind the sternum. His bowel movements were regular, once daily, with a laxative.

Physical examination showed considerable weight loss since the previous visit. The skin of the chest was browned and scaly. The blood pressure was 110/70. The remainder of the examination was unchanged.

The temperature, pulse and respirations were normal.

Examination of the blood showed a red cell count of 4,100,000, with a hemoglobin of 70 per cent. The white cell count was 9,000, 80 per cent polymorphonuclears. A stool examination was negative.

An x-ray showed a narrowing of the lumen of the esophagus at the site of the lesion. The esophagus remained filled while the patient was prone. In the upright position, however, the barium passed fairly well. The lesion was more sharply defined and appeared to involve the fundus of the stomach.

The patient was given further x-ray therapy. He refused other treatment and returned to his home in three days. He became gradually weaker, was able to eat less food and finally died two months after his final discharge.

Differential Diagnosis

Dr. Tracy B. Mallory: I have asked Dr. Means to start the presentation of this case and then turn it over when we come to the details of the esophagus to Dr. Mosher, who knows nothing about the case and will give a differential diagnosis from that aspect.

DR. J. H. MEANS: I will try to bring out the things that are important. This was a man I took care of in the Baker Memorial, followed through two diseases, and saw on Cape Cod last summer several times up to the time of his death.

The first admission had nothing to do with the final story so let us pass over it.

The repair of the hernia is of no interest at the present time.

Let us go to the third admission, when I first saw him, and consider that briefly.

The weight loss had been very gradual and did not indicate any wasting disease. The story abstracted from the Baker Memorial record is fairly clear, but as I got it verbally I got a still more vivid impression that it was a classical picture of coronary thrombosis of a mild sort. When he came to the hospital there were no symptoms whatever. He was kept in bed for four weeks simply as a precautionary measure because we believed he had coronary thrombosis.

As I recall, the cardiologist had thought the electrocardiographic findings were an indication of coronary thrombosis. He had another small attack of coronary pain in the hospital, not an impressive one, but yet a fairly typical attack of angina pectoris apparently. Since then he had no more symptoms of any kind pointing toward his heart; therefore, we can set that aside as chapter one. Of course, I saw the autopsy and I now know what this man had, but I did feel at the time, as anyone would, that he had had a small cardiac infarct. Subsequently I inferred that it was a well healed one because of the extraordinarily good result which followed. Chapter two has nothing to do with the coronary picture. When he came in the second time it was for a totally different disease. That is the one that interests us chiefly at present.

The history does not give us an accurate impression of this man's symptom picture. Doubtless this account was abstracted from the Baker Memorial history which the house officer took. I have no doubt that it is correct but it does not give the proper emphasis. The outstanding part of the picture was dysphagia. He had difficulty getting food down the esophagus into the stomach. This became apparent on talking with him. His sensation was of food sticking at the lower end of the sternum and after a time passing on into his stomach.

Am I right in supposing that this electrocardiogram still shows some evidence of coronary disease, Dr. Glendy?

DR. ROBERT E. GLENDY: Yes.

DR. MEANS: So, although he had no symptoms pointing to the coronary and had carried on a fairly normal existence he still had electrographic evidence that something had happened to the heart over a year before.

We might let the x-ray men state their findings at this point to make it interesting. They were not in entire agreement.

X-RAY INTERPRETATION

DR. AUBREY O. HAMPTON: This is the lower end of the esophagus and a herniated portion of the fundus of the stomach. Complete filling is not possible in the upright position. He was lying on the table drinking out of a tube as rapidly as possible when this film was taken. The left side of the diaphragm is here, the stomach there, the stomach comes through the diaphragm up to here and this we think is in the region of the cardiac sphincter. In this area near the cardiac sphincter there is a one centimeter fleck which we thought to be ulceration, and surrounding it is a large area of induration. There is also a diverticulum up here just below the arch of the aorta. I described this lesion as being rather unusual in that the ulceration was smaller than one would expect with a malignant lesion of this type. That is, the ulcer should be dish-shaped and its margins should be nearer to the periphery of the filling defect, and for this reason we asked Dr. Schatzki to see the patient.

DR. RICHARD SCHATZKI: The x-ray examination seemed simple until this moment and became complicated as soon as I looked at the patient. The reason was this: There were those changes just described by Dr. Hampton, the small hernia of the stomach through the hiatus, a diverticulum, and just above the cardia was this area of rigidity with a small area of ulceration, or rather this small constant fleck, but there was also pathology higher up in the esophagus above the diverticulum, almost to the arch of the aorta. Then the question arose as to what this lesion higher up was. In some of the pictures one saw definite band-like areas of decreased density running through this region. It was rather difficult to combine all these facts: pathologic changes extending over at least the lower half of the esophagus with increased rigidity in the lower end of the esophagus.

I finally reported that I had never seen a picture like this. The upper part of the picture looked more like varices than anything else but it was difficult to explain the rigidity of the lower end of the esophagus by this diagnosis. I had never seen a patient with difficulty in swallowing due to varices but if, at the time of the examination, I was forced to explain all the anatomical changes by one diagnosis I would favor varices though it was impossible to exclude cancer.

DIFFERENTIAL DIAGNOSIS CONTINUED

DR. HAMPTON: He did drink a little alcohol, did he not?

DR. MEANS: Yes, within reason. He was an artist.

The next event was the esophagoscopy and

Dr. Mosher is going to discuss the case at this point. He has had just the information that Dr. D. Campbell Smyth had when he did the esophagoscopy. The x-ray men were in some doubt as to what the lesion was and the suggestion was made by Dr. Schatzki that he had esophageal varices; and the picture, as Dr. Schatzki has said, is almost classical of that. There was no reason, however, that we could discover why he should have had esophageal varices. We had no evidence of cirrhosis of the liver.

Will you carry on, Dr. Mosher?

DR. HARRIS P. MOSHER: I am glad Dr. Means said something about this man's being an artist and mentioned his being human because as Dr. Means started out he implied that this was inconsequential from the scientific standpoint.

I was overcome with the elaborate history. It took half the morning to read it. I was very much pleased that the medical house officer missed the chief point, namely, that the man had difficulty in swallowing. This carries me back to my own house officers a little more cheerful than before I came over.

The chief feature in this case is that the man had difficulty in swallowing at his fourth admission, and in this connection he had abdominal pain. The examination by Dr. Smyth was practically typical of carcinoma and the report on the biopsy was epidermoid carcinoma. Thus it was a perfectly straight case.

The x-rays as you saw, and as Dr. Schatzki said, suggested varices. Dr. Schatzki was enthusiastic enough to come over and watch Dr. Smyth at the examination. He looked over Dr. Smyth's shoulder trembling and said he trembled more when Dr. Smyth took a specimen, thinking that Dr. Smyth was going to get into trouble from hemorrhage. This did not happen.

The points I wish to speak about are the pouch and hernia of the diaphragm. A pouch at the level of the arch of the aorta is extremely common. It is usually due to a suppurative gland which has become attached to the esophagus and in healing pulls it out into a pouch. It gives few symptoms. They are easily found with the esophagoscope. These pouches usually empty themselves and so, from the clinical standpoint, amount to very little.

Herniation of the stomach through the esophageal opening of the diaphragm was discovered, as the older men know, by Dr. Morrison of this city. Dr. Jones has operated on quite a few of these cases by mobilizing the lower end of the esophagus, pulling it down and fastening it. These hernias are fairly common, especially after sixty years, and cause very few symptoms, and are no longer operated upon.

The patient was treated by x-ray and swallowed better for a short time. This brings up the question of the treatment of carcinoma of the esophagus by x-ray. We have had two cases under treatment in this hospital with disappearance of the lesion. X-ray will cause the disappearance of the carcinoma, but the resulting fibrosis is apt to be a condition equally dangerous.

DR. A. S. MACMILLAN: My part will be limited to the showing of lantern slides on the relative frequency of carcinoma in patients with difficulty in swallowing. This slide was made from a careful study of 1,000 cases of dysphagia. It shows that carcinoma accounts for 40 per cent, and cardiospasm or, as Dr. Mosher has correctly labeled the condition, fibrosis of the lower end of the esophagus is second in frequency with 15 per cent. Other lesions that are to be found in the esophagus are webs, pouches, paralysis, burns, and ulcers. Varices of the esophagus while they may account for profuse hemorrhage do not produce obstruction. In the general classification of the causes of death in the United States, according to the government statistics, carcinoma of the esophagus is low in the list, accounting for only 1.5 per 100,000, while 21.4 per 100,000 cancers occur in the stomach. Carcinoma of the esophagus occurs, as you would expect, at the same time as carcinoma in other parts of the body; the average age in our three hundred and eighty patients was sixty-seven, with very few in the third or fourth decade.

DR. MEANS: There is very little more to add. Dr. Hampton gave this man a course of heavy radiation, as heavy as he knew how to give.

DR. HAMPTON: We gave him 8000r, 2000r to each of four fields 10 by 20 centimeters in size directed to the lower half of the esophagus. He had no discomfort from these treatments. As a matter of fact, he ate an elaborate dinner during the treatments and said he had some champagne, too. He felt quite well. Following these treatments the tumor in the esophagus did smooth out and we thought that there was less delay in the passage of barium through the esophagus, although there was not much delay in the first place. At the second entry after the x-ray treatment we thought the lesion looked the same as in the beginning. We gave him another series of treatments equal to the first and, so far as I can tell, without injuring his skin appreciably.

DR. MEANS: He went downhill rapidly with esophageal cancer and died. Gastrostomy, which was offered to him, he refused, I think quite wisely, and with morphia was made comfortable. He never had pain at all, had gradually increasing dysphagia, and finally got to the point where he was bothered with swallowing mucus, having that collect and being obliged to vomit it up. I talked to Dr. Mixter about gastrostomy who said the chief reason for do-

ing it was to relieve the pangs of hunger. If they were troublesome, as they may be, gastrostomy offers relief. This patient did not complain of that and it was not necessary. He gradually became more and more emaciated and finally died of weakness.

Clinical Diagnoses

Carcinoma of the esophagus.
Coronary heart disease.

Dr. Harris P. Mosher's Diagnoses

Epidermoid carcinoma of the esophagus.
Diverticulum of the esophagus.

Anatomic Diagnoses

Adenoacanthoma of the esophagus with metastases to the tracheal and esophageal glands and lungs.
Diverticulum of the esophagus.
Arteriosclerosis, marked; aortic, coronary, renal.
Bronchopneumonia.
Pulmonary congestion.
Cholelithiasis.
Cachexia.

Pathologic Discussion

Dr. Mallory: When the second phase of this man's illness developed the history was a fairly obvious one of cancer of the esophagus and I do not suppose there would have been any question of diagnosis at all if Dr. Schatzki had not been brought into the case. Dr. Schatzki found this quite extraordinary picture which was inconsistent with anything anyone had seen in cancer of the esophagus. The autopsy specimen shows very clearly why that was the case. We found an extensive tumor in the lower third of the esophagus, close to the cardiac orifice. Then the mucosa of the esophagus for the most of its middle third was elevated by papillary masses of tumor. Looking at it from the surface one would suppose that he was dealing with a papilloma of squamous epithelium, rather similar to what one sees in the bladder. Microscopic examination shows something entirely different, however. The tumor proves to be an adenocarcinoma although in places there is a little bit of cornification and you can call it adenoacanthoma if you want to. It is invading all layers of the esophageal wall, the submucosa, the muscularis, and the serosa. It crops up to the surface from below the various spots, but even where these shaggy papillary masses are most marked there is a layer of normal epithelium above the tumor, so the situation is exactly analogous to that seen with varices; a hidden mass in the submucosa pushes the true mucosa upward and it is only reasonable that an x-ray picture identical with varices should have been produced.

With regard to the rest of the autopsy, we found almost complete occlusion of the descending branch of the left coronary, evidently quite old and calcified, but we were not able to find any gross evidence of infarction of the myocardium.

Dr. Hampton: The biopsy was taken eleven inches from the teeth. I think the large lesion that we first found was fourteen inches from the teeth.

Dr. Mallory: Adenocarcinomata are less common than squamous carcinomata and when found are usually at the lower end of the esophagus, close to the cardiac orifice. I think there is little question that the tumor started close to the cardia and gradually worked its way upward through the lymphatics and perineurial spaces, possibly in part through the blood vessels.

Dr. George W. Holmes: Is this condition of extension by cancer up along the esophagus giving the appearance you describe generally known to pathologists?

Dr. Mallory: It certainly was not known to me. I had never heard of it. Do you know of any cases, Dr. Mosher?

Dr. Mosher: No.

CASE 21522

Presentation of Case

First Admission. A sixty-nine year old white American woman was admitted because of an injury to the back following a fall.

Physical examination showed a rather obese elderly woman lying quietly in bed. The heart appeared to be normal. A_2 was greater than P_2. The blood pressure was 175/80. A few fine râles were audible at both lung bases. There was a point of tenderness over the eighth dorsal vertebral spine and marked spasm of the erector spinae muscles. No attempt was made to elicit spinal movement. All normal reflexes were present and unaffected. A sensory examination was negative.

An x-ray examination showed a collapsed fracture in the region of the fourth and eighth dorsal vertebrae.

A high back brace was applied and the patient was discharged on the fortieth hospital day still wearing the back brace and suffering no marked discomfort.

Second Admission, two years later.

The patient had been seen in the clinic many times following her discharge. She was treated there palliatively for complaints which concerned themselves for the most part with lower abdominal pain, cramps, constipation, and painful stiff joints of long standing. She had been

seen at another hospital five months prior to her reëntry where she complained of "chest pain, heart attacks, attacks of cough, and shortness of breath". Hospitalization was advised but the patient returned to her home.

At 3:00 a.m. on the morning of her reëntry she was awakened by a severe pain in her epigastrium and lower chest, radiating to the region between her shoulder blades. There was also pain in both upper quadrants. The patient's condition was such that further details could not be elicited. The pain continued unabated until 7:30 a.m., when the patient came to the hospital in a taxicab.

Physical examination showed a poorly nourished elderly woman evidently suffering from considerable pain. She was restless and uncoöperative, and her condition precluded further examination. There was no cyanosis. The heart sounds were of poor quality and were slightly accelerated. The blood pressure was 100/60. There was marked tenderness in both upper quadrants. It was particularly excruciating on the left. The liver edge was thought to be palpable three centimeters beneath the costal margin.

The temperature was 98.6°, the pulse 90. The respirations were 20.

Ten minutes after examination the patient became intensely cyanotic, her neck veins became markedly engorged, and she died within a few minutes.

Differential Diagnosis

Dr. Sylvester McGinn: On the first admission there are three points that stand out. One is that we can establish the normal blood pressure as 175/80. The second is that she was having early signs of congestive failure marked by fine râles at both lung bases. The third is an injury to two vertebrae.

"She had been seen at another hospital five months prior to her reëntry where she complained of 'chest pain, heart attacks, attacks of cough, and shortness of breath.'" There is an important bit of evidence here. We would like to know what the chest pain was, whether it was precordial discomfort or the chest pain of angina coming on exertion, and what the heart attacks were like. Were they paroxysmal attacks of tachycardia or did they relate again to the anginal syndrome? The fact that hospitalization was suggested and advised makes me think that she had a considerable degree of cardiac involvement at the time. I think we must assume that.

In summary, we have an elderly woman who had been definitely having attacks of heart trouble, probably with congestive failure and, I believe, with angina, having an attack at night and dying about five hours later. I think it is fair to assume that the attack she had at three o'clock was the beginning of the final episode five hours later. There are abdominal symptoms with reference of pain to the midscapular region suggesting gallbladder disease. I do not believe that people can die that suddenly of gallbladder disease. A cerebral accident causing sudden death is another possibility. She had five hours to develop some kind of neurological symptoms and I think we would have been told if there were any present. Sudden death can come in aortic stenosis and I believe if she died from aortic stenosis we would have been given more information if murmurs had been present. Sudden death is observed in cardiovascular syphilis, either from involvement of the coronary vessels or rupture of an aneurysm. That is a possibility, but I think the three most likely possibilities are those of coronary thrombosis, pulmonary embolism or dissecting aneurysm. We have a real lead for dissecting aneurysm here, in that the pain is definitely referred to the midscapular region and if there is any one single point we have in looking for dissecting aneurysm of the aorta it is this presence of midscapular pain. Death was marked by venous engorgement. If she had a dissection beginning at three in the morning and rupturing five hours later I believe that she probably would have been bled out rather than have engorgement of the neck veins, unless there was a cardiac tamponade where rupture had taken place into the pericardium. In view of the past history, I do not think that is quite so likely as the two conditions that are left, pulmonary embolism and coronary thrombosis.

At three o'clock something happened to give her a definite drop in blood pressure, from 175/80 to 100/60. She was not definitely cyanotic when she came into the hospital but that is not particularly against pulmonary embolism because with the initial embolus patients often go into shock and are seen without venous engorgement and without cyanosis. I do not know whether an embolus could occur so late from the effects of the neck injury, but it must be included. There is another possible location for a thrombus and subsequent embolus. The liver was three fingers down, indicating well-marked congestion and in any such case thrombi in the larger systemic veins are frequent and would provide sources for an embolus.

The final possibility is coronary thrombosis. It is an atypical condition where the pain is especially noticed in the abdomen and yet that can occur. A reference of the pain to the midscapular region would be consistent with a right coronary occlusion. I saw one case of coronary occlusion, occurring in the hospital, where all the symptoms were related to the lower abdomen, in the region of the pelvis, and it was some time later before the pain ever did get up into the chest. Rupture of the heart is strongly suggested by the terminal symptoms though

the time interval seems short. Again it is possible to have a pulmonary embolism after a coronary thrombosis as a result of a mural thrombus, and yet five hours seems a short time for a clot to have formed.

I think, in view of the past history and believing that the attacks of chest pain were anginal, that she had a coronary thrombosis, probably with rupture of the heart into the pericardium.

Dr. Gerald Blake: The contrast between the patient's appearance ten minutes before death and immediately after death, particularly the engorgement of veins in the neck, suggest failure of the right heart. It is perhaps better explained by pulmonary embolism. But we have no story of previous infarction of the right heart, and it is too early for this attack to produce an embolus from a mural thrombus. My thought was that this patient had coronary thrombosis, probably in the right coronary.

Dr. Paul D. White: May I add a comment about rupture of the heart? It seems to me very unlikely if the coronary thrombosis which is the probable diagnosis here occurred at three a. m. that the heart could have ruptured that same day; the cases of heart wall rupture from coronary thrombosis that I remember generally occurred in the second week or between about five and seventeen days after the acute coronary occlusion.

Clinical Diagnosis

Coronary thrombosis.

Dr. Sylvester McGinn's Diagnoses

Acute coronary thrombosis, possibly with rupture of the heart into pericardium.

Anatomic Diagnoses

Coronary thrombosis with occlusion, fresh.
Infarct of heart, old.
Arteriosclerosis, marked: Coronary, aortic, renal.
Peritonitis, chronic, generalized.
Hydrothorax, very slight, bilateral.
Pulmonary tuberculosis, healed, right apex.
Cholelithiasis.

Pathologic Discussion

Dr. Tracy B. Mallory: I think the earliest case of rupture that I have seen occurred three days after the thrombosis. They are usually later than that. This patient did show a coronary thrombosis but it was in the usual spot, the descending branch of the left coronary artery and not the right. There was no gross evidence of infarct of the heart, as you would expect in a case dying within four or five hours of the time of onset. It takes a definite length of time before degenerative changes become visible, even microscopically several hours are required. The patient, like a good many cases of coronary thrombosis, had apparently had one before. We found one small area of healed infarction, an old fibrous scar, evidently years old, to which there is no lead whatever in her past history.

Dr. McGinn: How long does it take for a mural thrombus to form, and how long before an embolus can be given off? Can a fat embolus or clot arise from an injury two years old?

Dr. Mallory: It seems unlikely without some succeeding, recent trauma. One does, of course, from time to time see a sudden pulmonary embolus in a medical patient in whom there is no history whatever of phlebitis, and no lead as to the possible source of emboli. As a matter of fact small emboli, according to Dr. Belt of Toronto, are probably commoner in medical cases than in surgical cases. The very massive embolus that is rapidly fatal, however, seems to be pretty rare in medical as compared with surgical cases.

In regard to the rapidity of formation of a thrombus, I do not know of any exact figures. I should guess that it would take forty-eight hours perhaps before the thrombus formed, but that is nothing more than a guess, and probably some little time after it is formed before it is likely to break loose and give rise to an embolus.

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WHO IS INTERESTED IN RAISING THE STANDARDS FOR PRACTICE?

IF the question concerning interest in raising standards of qualification for the practice of medicine in Massachusetts is phrased "Who is interested?" one finds signs of concern for or against such raising on the part of a few persons only. The Board of Registration in Medicine regularly puts itself on record by recommending to the General Court each year that the standards be raised. The Massachusetts Medical Society puts itself on record as favoring such raising. The proprietors of low grade medical schools, or their representatives, put themselves on record as opposed to raising standards. The members of the General Court apparently take little interest in the matter and express themselves as satisfied with the status in quo.

The opposition states that the Board is interested in increasing its own power; that the Medical Society is interested in limiting practice to persons of whom it approves. In other words the "Haves" are trying to keep out the "Have nots". The proprietors of the objecting schools are seeking to preserve their vested interests since they are reported to be making money under present conditions.

But to whose interest is it that the standards of medical practice be raised? To the Board? Yes, because its prime function is to protect the public against incompetent practitioners of medicine, and its members know that mere graduation from a medical school is no guarantee of competence. To the medical profession? Yes, because it is a profession and its prime function is to render a service and not to make money. To the General Court? Yes, because its prime function is to make the laws by the administration of which the people of the Commonwealth are protected against incompetent practitioners of medicine. It seems to be satisfied with the status in quo because the legislators appear to be impressed by the persons who make the most noise; magnitude of noise directs their thinking.

The medical schools reported to be making money? Their answer is equivocal: no, in so far as they are interested in making money; yes, in so far as they are interested in education. The equivocation is due to the fact that medical education is expensive and costs more than students pay. Since actions speak louder than words, the interest in education becomes inconsiderable and the worship of mammon makes the welkin ring.

What is for the interest of the people, who are sick, many of whom, medically speaking, do not know their left hand from their right? Should they not have the best medical care there is? Is not every human being entitled to the best possible medical care? Yes, and the problem is the practical one of making it available.

If raising the statutory standards for admission to the practice of medicine will actually improve medical care in the state, what justification is there for not changing the statute? Should revenue derived from giving an inadequate medical education be allowed to stand in the way of better medical care for the people of Massachusetts?

But who lifts a voice that can be heard all over the state on behalf of the sick of the state? The Board mildly recommends. The Medical Society mildly approves the recommendation. The General Court is complacent since the people do not speak for themselves. Who will be a Moses to this people?

PRACTITIONERS, WAKE UP!

IN June, 1935, upon the recommendation of the Committee on Public Relations of the Massachusetts Medical Society, the Council of

the Society voted to urge the various boards of health and health officers throughout the Commonwealth to refrain from establishing clinics and doing immunization work against diphtheria for people who are able to pay for that work, except in cases of emergency.

At the same time upon recommendation by the same committee, the Council voted to urge the practitioners of medicine to organize for immunization work at an appropriate cost to the public.

In making these recommendations, the committee felt that on this program the practitioners would be stimulated to be more of a force in the problems of preventive medicine and the patients would be better served in having this work done by the family physician.

These votes have been spread throughout the Commonwealth and already some misgivings have been voiced by health officers that this immunization work against diphtheria will diminish if the health officers do not continue their clinics for this work. The figures which are obtainable suggest that where at the request of the practitioners the health authorities have not done this work, the immunization work is not done. Another feature of this problem is that there is the need of educating the public in regard to the value of this work, and experience indicates that persuading an individual to adopt a new idea is more difficult if there is expense attached to it.

If the health officers are going to give up immunization against diphtheria, the practitioners must not simply immunize those who apply, but must aid in educating the public in regard to the importance of eliminating diphtheria from the Commonwealth. An aggressive attitude rather than a passive one toward bringing patients into physicians' offices for this work should be organized and pronounced ethical. Arrangements should also be made so that patients may receive this immunization at a price commensurate with their ability to pay. Unless the practitioners wake up and do this work, the misgivings of health officers will be justified and the work should be turned back to them.

It is of interest to note that the physicians of Boston as represented by the members of the Middlesex South, Norfolk and Suffolk District Societies have already organized to offer opportunities for immunization at a rate much below the usual price of office visits and that the health officers of the City are urging the patients to go to their family physicians for this work.

Let us hope that this experiment will succeed and that throughout the Commonwealth the practitioners and health officers will coöperate in developing similar programs.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

LAHEY, FRANK H. M.D. Harvard University Medical School 1904. F.A.C.S. Director, Lahey Clinic. Surgeon-in-Chief, New England Baptist Hospital. Surgeon, New England Deaconess Hospital. Address: 605 Commonwealth Avenue, Boston. Associated with him is

SWINTON, NEIL. M.D. University of Michigan Medical School 1929. Surgeon, Lahey Clinic. Address: 605 Commonwealth Avenue, Boston. Their subject is "Stones in the Common and Hepatic Bile Ducts." Page 1275.

VIETS, HENRY R. B.Sc., M.D. Harvard University Medical School 1916. Instructor in Neurology, Harvard University Medical School. Neurologist, Massachusetts General Hospital. Consulting Neurologist, Massachusetts Eye and Ear Infirmary. Address: 6 Commonwealth Avenue, Boston. Associated with him is

SCHWAB, ROBERT S. M.D. Harvard University Medical School 1931. Assistant in Neurology, Harvard University Medical School. Resident in Neurology, Massachusetts General Hospital. Address: Massachusetts General Hospital, Boston. Their subject is "Prostigmin in the Diagnosis of Myasthenia Gravis." Page 1280.

DEWITT, R. F. B.S., D.N.B., M.D. University of Vermont College of Medicine 1934. His subject is "A Recent Outbreak of Food Poisoning in Shoreham, Vermont." Page 1283. Address: Plymouth, N. H.

WADSWORTH, AUGUSTUS B. B.S., M.D. College of Physicians and Surgeons, Columbia University 1896. Assistant in Bacteriology and Hygiene, 1899-1908; Assistant Professor of Bacteriology, 1908-1913; College of Physicians and Surgeons, Columbia University. Director, Division of Laboratories and Research, New York State Department of Health, Albany, 1914-. His subject is "Practical Limitations of Vaccine and Serum Therapy." Page 1285. Address: Division of Laboratories and Research, New York State Department of Health, Albany, New York.

MCGINN, SYLVESTER. A.B., M.D. Harvard University Medical School 1929. Assistant in Medicine, Massachusetts General Hospital. Staff, St. Elizabeth's Hospital. Cardiac Consultant, Sturdy Memorial Hospital, Attleboro. His subject is "Progress in the Study of Cardiovascular Disease in 1934." Page 1293. Address: 270 Commonwealth Avenue, Boston.

The Massachusetts Medical Society

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PYELITIS AND PREGNANCY

The past two decades have contributed materially to our knowledge concerning, and management of, nontuberculous infections associated with pregnancy. They still remain in two major divisions, namely, infections present during gestation and infections which follow delivery.

Both subdivisions are influenced by the physiological changes in the bladder, ureters and pelves, which are generally admitted to take place to some degree, in all pregnant women. These changes modify the incidence of infection during the pregnancy. They occur in approximately one and a half per cent of all pregnant women, which is well above the incidence of such infections in nonpregnant women. They also modify the character of postdelivery infections if they occur, as they usually do, before the retrogressive changes in these organs, which begin immediately after delivery, have had time for completion.

The changes which occur in the bladder and urethral walls during pregnancy apparently are of little significance. Residual urine is absent except with cystocele or gross urinary pathology. Malformation of the bladder from pressure of the uterus produces nothing worse than a benign form of frequency, which is free from symptoms of stranguria. It is worthy of remark that burning and painful voiding is less common in these bladders, when infection is present, than in the nonpregnant. Absence of this symptom confuses differential diagnosis in many cases of fever.

Changes in the upper urinary tract, due to pregnancy, are of great significance in modifying the symptomatology and management of infections which occur either in the course of pregnancy or immediately after delivery. The characteristic deformity is dilatation of the upper two thirds of the ureters and the pelves. The midportion of the ureter is carried laterally and redundancy of ureteral length is taken up in kinking near the renal pelvis and near the pelvic brim. The pelvis dilates extensively and rounded calyces are often noted which suggest a long-standing condition, but which return to normal in the course of the retrogression which follows delivery. Deductions made from pyelography, performed during the stage of dilatation, are unsafe findings on which to do radical surgery. These dilatations are accompanied by atony which accounts for the often painless character of the condition and the persistence of dilatability after delivery without the usual pain response to overdistention, so noticeable in the normal kidney. Atony may also be responsible for the severity of postpartum infections of the kidney since edema of the more nearly unchanged lower portions of the ureters may produce retentions in the dilated portion and pelvis above.

While hematuria marks the onset of pyelitis in pregnancy, in a sizable group of cases, and others show only fever and pyuria, dull renal pain, fever, nausea and rapid pulse, with or without bladder symptoms, are the usual symptoms. Acute appendicitis and pelvic peritonitis constitute the common differential diagnosis. Pelvic peritonitis increases in importance in differential diagnosis in the postpartum infections. The white cell count is usually in the neighborhood of 15,000 in urinary infections and higher in the other diseases but is not always reliable.

The state of nutrition and secondary anemia are important considerations both as to incidence of infections and their management. Transfusions are not used in the course of pregnancy as treatment for anemia in most clinics but are freely used in the postpartum stage. Blood-building diet and preparations of iron will suffice in most instances to combat anemia in pregnancy when coupled with proper urologic measures where required.

The treatment of pyelitis in pregnancy should begin with the pregnancy. Where free ingestion of fluid is practiced with all pregnant women, those infections which occur are less toxic in character. Ten to fifteen glasses of water daily are advised. The onset of infection in patients with low fluid intake is quickly marked by severe degrees of toxicity and with sustained nausea. The patient quickly becomes seriously ill and unresponsive to treatment by any means until fluids have been restored in large quantities by other means.

Rest in bed, forced fluids and alkalinization by oral or rectal means are adequate measures for handling the majority of infections in pregnancy. Elevation of the foot of the bed and changing the patient from one side to the other have proved effective in both the pregnant and the nonpregnant in shortening the febrile period. Sixty grains of potassium citrate is adequate alkalinization for the average case. PH determinations on the urine will control the medication.

If conservative measures do not produce evidence of beginning subsidence of pulse and

*A series of short selected articles by members of the Section is being published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the Section.

temperature by the fourth day, cystoscopic measures should be considered. Of the two signs the pulse is a more reliable indication of the patient's condition than temperature. Beyond the fourth and fifth days, patients are more resistant to treatment by cystoscopic measures.

Cystoscopic treatment, early in the infection, is productive of prompt amelioration of symptoms when it consists of nothing more than emptying the pelves, allowing them to drain for fifteen to twenty minutes and washing them clear of pus with a bland solution such as two per cent boracic acid solution. If symptoms recur, this can be repeated at three-day intervals. Cystoscopic treatment can be expected to fail in the long-standing septic case of weeks' or months' duration. Inlying ureteral catheters are not required in cases treated early in the disease. They have several disadvantages, they require special and constant care to prevent plugging with pus and mucus, they are painful for the patient, and produce edema of the lower ureteral segment by their presence. After removal this edema is, in itself, obstructive.

There will be found a few intractable cases which are best treated either by interruption of the pregnancy or surgery. Unless there is some unusual reason to the contrary, interruption is advised. The insertion of a pezzer tube in the pelvis, which can be worn throughout the remainder of the pregnancy, will preserve the first pregnancy but becomes less attractive for subsequent infected pregnancies should they occur. These sinuses heal promptly after delivery.

Postpartum bladder dysfunction is closely associated with postpartum pyelitis. Perfectly adequate and timely management of the bladder after delivery should, theoretically, abolish postpartum pyelitis. This is not easy to accomplish. Trauma to the bladder at delivery and probably other factors result in either complete retention of urine or overflow from a residual. In palpation of the abdomen it is not easy to differentiate the bladder and the uterus immediately after delivery. When in doubt catheterize. Frequent voiding of small amounts of urine indicates residual. Bladder management is carried on by one of two adequate measures, intermittent catheterization or constant drainage. If infection exists previous to delivery, constant drainage with the pezzer type of catheter (not soft-winged catheters) is preferable to intermittent catheterization. The onset of retention will often produce symptoms of pyelitis within a few hours in the infected case, but in the uninfected case infection must be introduced, and time allowed for its development, before a pyelitis is apt to occur. If uninfected, catheter relief should be tried for either residual or retention for a period of four or five days. In those cases in which the residual or retention is not allowed to exceed twenty to twenty-five ounces, fevers seldom occur. Catheterization must be controlled by the fluid output rather than the clock. Bladders which distend to large urine content between catheterizations have little chance to overcome atony. If constant drainage is placed it should be left undisturbed for five days. This period has been determined empirically. After removal, the bladder should be checked for residual. If large the catheter should be replaced for another five-day period. Two to three ounce residuals are usually handled safely by the patient, but should be watched. Constant drainage is preferable for the resistant case, because it requires less constant exercise of judgment to insure against inadequate emptying of the infected bladder.

Intravenous pyelography is eminently satisfactory in pregnancy and the puerperium. It should be resorted to early in pregnancy, where there is any suspicion of preëxisting pathology in the urinary tract. It is safer for both mother and child to carry a patient through pregnancy with *known* handicaps present, than to try to rush to a diagnosis, as an emergency, after trouble has arisen. Early diagnosis of preëxisting pathology can be made without undue x-ray exposure at any time in pregnancy.

In the majority of instances the patient will complete the pregnancy safely. If this is to be accomplished, at the cost of destroying one or both kidneys, there must be an accounting of values, preferably made as early as possible in the pregnancy. Where the lesion is producing no real damage it can be remedied after delivery. This applies to most stones. Pregnancy cases tolerate any urological operation well if liberally supplied with morphine during convalescence.

Pure cystitis, without renal involvement following intermittent catheterization or constant drainage for bladder atony, is usually bacteria and pus free in thirty days. The average renal infection is free in four months. Failure to clear in that time under treatment should lead to cystoscopic investigation. It is assumed that the general condition of the patient, anemia, social aspect of her life, and formalin bearing drugs given with a urine having a pH of at most 5 have already been considered and proper relief measures applied.

It is unfortunate that symptomatic recovery so readily follows delivery. Unless the patient is bacteria free, an infected subsequent pregnancy is practically assured.

OUR RESPECTED SENIOR FELLOW

In 1868 Dr. Edmund Horace Stevens of Cambridge, Massachusetts joined the Massachusetts Medical Society, and on January 2, 1936, will celebrate his ninetieth birthday.

It is eminently fitting that the members of the

Society should take cognizance of the record and influence of this, our Senior Fellow, and do him the simple honor of a brief reference to his accomplishments.

Dr. Edmund Horace Stevens was born January 2, 1846, at Stanstead, Quebec, Canada, the son of Dr. Horace and Louisa Mann Stevens. Both his father and mother were of old New England stock, their forbears having come to Massachusetts between 1630 and 1640. Dr. Horace Stevens had graduated from the Vermont College of Medicine in 1842 and settled in Stanstead shortly after that. In 1848 the family moved to Skowhegan, Maine, and there Dr. Edmund H. Stevens lived through his boyhood, attending the local schools and Bloomfield Academy.

In 1861 he entered Dummer Academy in South Byfield, Mass., and remained there until early in 1863 when he was forced to leave school on account of ill health. At that time he, supposedly doomed to an early death from tuberculosis, was put in the care of Dr. Henry I. Bowditch. He remained in Boston in Dr. Bowditch's care and in the fall of 1863 registered as a student under Dr. James Harlow and began to attend lectures at the Harvard Medical School. In May, 1864, he enrolled in the Navy as medical cadet and was assigned to the U. S. S. Philippi, attached to Farragut's fleet. In August, 1864, at the Battle of Mobile Bay, while under shell fire from the forts, he sustained a broken leg from a flying splinter and was invalided home.

In September of that year he formally entered the Harvard Medical School. In March 1865 he entered the Army as a contract surgeon and was assigned to duty to the Cavalry Post Hospital at City Point, Virginia, where his father was in command. He was mustered out of the army in July, 1865, and returned to Boston to resume his studies. He graduated from the Harvard Medical School in 1867 and in that same year was appointed Assistant Port Physician of Boston, stationed at Deer Island. He continued in this position until April, 1871, when he settled in Cambridge, where he has remained and practised ever since.

In 1886 when the Cambridge Hospital was opened he was the first Visiting Surgeon to go on duty and he continued to hold the position as Visiting Surgeon in that hospital until 1911, when he resigned and was appointed Consulting Surgeon which position he has since held.

He has been a member of the Massachusetts Medical Society since 1868, and was a Councilor from the Middlesex South District for about fifty years and nominating Councilor for many years. He has been a Fellow of the American College of Surgeons since its organization and one of the original members of the New England Surgical Society. He is also a member of the Boston Obstetrical Society, the New England Obstetrical and Gynecological Society and the Cambridge Medical Improvement Society.

During the World War he was a member of the Volunteer Medical Service Corps and of the Medical Advisory Board for his district.

Of Dr. Stevens' work both the profession and the laity have repeatedly testified. The writer recalls a statement of the late Dr. Frederick C. Shattuck, when doctors were under discussion, that he, Dr. Shattuck, would feel as safe in Dr. Stevens' hands, if obliged to submit to a surgical operation, as he would with any other surgeon. Coming from this eminent teacher and practitioner anything further would be superfluous.

Dr. Stevens' interest in the Massachusetts Medical Society is shown particularly in his disinclination to take advantage of the provision for retirement.

The *Journal* tenders its cordial congratulations to Dr. Stevens for his long and successful service to humanity with the wish for many more years of active life.

THE DIRECTORY OF THE MASSACHUSETTS MEDICAL SOCIETY

This publication is being compiled with all available information up to January 1, 1936. The material will be in the hands of the printer immediately after the first of the year and the copies will be distributed as soon as possible.

MISCELLANY

CHANGES AT THE MASSACHUSETTS MEMORIAL HOSPITALS AND BOSTON UNIVERSITY SCHOOL OF MEDICINE

The Trustees of the Massachusetts Memorial Hospitals have announced the following important appointments to the Staff:

Reginald Fitz, M.D., to be Director of the Robert Dawson Evans Memorial Department for Clinical Research and Preventive Medicine, and Howard M. Clute, M.D., to be Chief of the Surgical Service. These two appointments, when considered in connection with the completion of the new wing at the Main Hospital, constitute an important accomplishment for the year 1935 and the Trustees and Staff are to be congratulated. These appointments to the Hospital Staff carry with them professorial rank in Boston University School of Medicine and, since the new wing will add materially to the bed capacity of the Hospital, the clinical teaching facilities of the School will be considerably enhanced.

Dr. Reginald Fitz was born in Boston, received his A.B. degree from Harvard College, and his M.D. degree from Harvard Medical School in 1909. He served as house officer at the Massachusetts General Hospital and was later a voluntary assistant in the medical clinic of the Johns Hopkins Hospital. Following an appointment at the Peter Bent Brigham Hospital, he was an assistant resident physician at the Rockefeller Institute and later was an associate in medicine at the Massachusetts General Hospital. In 1920 to 1922, following an extensive army service in France, he was in charge of

the clinical section in medicine at the Mayo Clinic in Rochester, Minnesota, and after his return to Boston was appointed to the Staff of the Peter Bent Brigham Hospital and was made Associate Professor of Medicine at the Harvard Medical School. He is a member of the Association of American Physicians, the American Society for Clinical Investigation and a Fellow of the Massachusetts Medical Society and the American Medical Association. He is a member of the National Board of Medical Examiners, a member of the Council on Medical Education and Hospitals of the American Medical Association and is Chairman of the Committee on Medical Education and Medical Diplomas of the Massachusetts Medical Society. His wide clinical experience, and his interest in medical research and education make his appointment particularly significant at this time.

Dr. Howard M. Clute was born in Maine, received his S.B. degree from Dartmouth College in 1911 and his M.D. degree from Dartmouth Medical School in 1914. He served his internships at the Hitchcock Hospital in Hanover and the Boston City Hospital in Boston. For a number of years he has been associated with the Lahey Clinic of Boston and holds appointments on the Staffs of the New England Deaconess and the New England Baptist Hospitals and more recently has been Chief of the Surgical Staff at the Carney Hospital. He is a member of the American Urological Association, the New England Surgical Society, the Boston Surgical Society, a Fellow of the American College of Surgeons, and a Fellow of the Massachusetts Medical Society and the American Medical Association. Dr. Clute has been particularly active in the field of general surgery and has written on numerous surgical topics.

The new addition to the Massachusetts Memorial Hospitals completes a thoroughly modern plant with a unique arrangement of operating rooms and an up-to-date x-ray department. The private rooms and the facilities for patients of moderate means are particularly attractive.

TWO ADDRESSES BY DR. PHANEUF IN LOS ANGELES

Dr. Louis E. Phaneuf, professor of gynecology at Tufts College Medical School, addressed the Los Angeles Obstetrical and Gynecological Society on The Low or Cervical Cesarean Section, on December 11, and on December 13 gave the annual address before the Los Angeles Surgical Society, his subject being The Surgical Management of Prolapse of the Uterus and Vagina.

AN HONOR TO DR. BARBARA T. RING

As one feature of the exercises during the meeting of the New England Physical Therapy Society at the Ring Sanatorium, an honorary life fellowship was awarded to Dr. Barbara T. Ring as a tribute to the late Dr. Arthur H. Ring and for their contributions to the activities of the Society.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR NOVEMBER, 1935

Disease	Nov. 1935	Nov. 1934	5 Yr. Average*
Anterior Poliomyelitis	58	7	25
Chickenpox	861	1324	1027
Dog Bite	654	554	381
Epidemic Cerebrospinal Meningitis	5	2	7
German Measles	94	102	57
Gonorrhea	476	596	553
Lobar Pneumonia	248	262	291
Measles	303	326	528
Mumps	674	183	320
Scarlet Fever	756	599	782
Syphilis	464	390	344
Tuberculosis, Pulmonary	257	281	318
Tuberculosis, Other Forms	28	33	37
Typhoid Fever	7	10	15
Undulant Fever	2	3	
Whooping Cough	274	642	643

*Based on the figures for the preceding 5 years.

RARE DISEASES

Anterior poliomyelitis was reported from Belmont, 1; Beverly, 1; Boston, 9; Brockton, 5; Cambridge, 3; Canton, 1; Chelsea, 1; Concord, 2; Danvers, 1; Fall River, 4; Lawrence, 2; Lynn, 4; Malden, 1; Medway, 1; Melrose, 2; Methuen, 2; Middleton, 1; Montague, 1; Newton, 3; Revere, 1; Salem, 3; Somerville, 1; Swampscott, 1; Wareham, 2; Worcester, 5; total, 58.

Diphtheria was reported from Boston, 8; Canton, 1; Chelsea, 1; Chicopee, 5; Fall River, 2; Lawrence, 2; Lowell, 10; New Bedford, 2; Peabody, 1; Revere, 1; Somerville, 1; Taunton, 1; Watertown, 1; Total, 36.

Dysentery (amebic) was reported from Cambridge, 1.

Dysentery (bacillary) was reported from Medfield, 1.

Encephalitis lethargica was reported from Springfield, 1.

Epidemic cerebrospinal meningitis was reported from Boston, 1; Everett, 1; New Bedford, 1; Revere, 1; Worcester, 1; total, 5.

Malaria was reported from Abington, 1; Brockton, 1; Cambridge, 1; total, 3.

Paratyphoid fever was reported from Haverhill, 1; Tewksbury, 1; total, 2.

Septic sore throat was reported from Boston, 3; Chicopee, 3; Foxboro, 1; Lowell, 1; Shirley, 1; total, 9.

Tetanus was reported from Nantucket, 1; Taunton, 1; total, 2.

Trachoma was reported from Lexington, 1; Medford, 1; total, 2.

Trichinosis was reported from Brockton, 1; Easthampton, 2; total, 3.

Typhoid fever was reported from Chicopee, 1; Fall River, 1; North Andover, 1; Springfield, 1; Walpole, 1; Waltham, 1; Westport, 1; total, 7.

Undulant fever was reported from North Adams, 1, Pittsfield, 1; total, 2.

There have been fewer reported diphtheria cases for the year to date than there were in the month of November, 1929.

Typhoid fever remains well below last year's record low figure.

Infantile paralysis continues to decline after a season of increased prevalence.

Lobar pneumonia for the first time since March was reported at a lower level than for the corresponding month of 1934.

Epidemic cerebrospinal meningitis occurred to about normal expectancy after a month of somewhat increased prevalence in October.

Scarlet fever for the second consecutive month was reported at a higher figure than in 1934.

German measles, measles, tuberculosis other forms, and chickenpox were not remarkable.

Pulmonary tuberculosis remained below the five-year average for the month.

Whooping cough continues to run low, while mumps maintains its increased incidence over last year.

CORRESPONDENCE

DIATHERMY IN LOBAR PNEUMONIA

Editor, *New England Journal of Medicine*,

The article by Drs. Wetherbee, Foley and Resnik, entitled "*Diathermy in Lobar Pneumonia*", published in the *New England Journal of Medicine*, October 24, 1935, has attracted the attention of men interested in the pneumonia problem. It has, therefore, seemed worth while to make a careful analysis of the data presented. As a result of such a study I should like to make the following points:

1. The authors' plea for the use of diathermy is based in part on their belief that the specific pneumococcus antiserum has not been shown to be effective. They base this conclusion on the comparison of mortality rates for pneumonia at the Boston City Hospital in 1901 with the mortality rates reported by Dr. Stewart in 1934. The City Hospital series comprised 900 pneumonia patients who were reported by Sears and Larrabee to have shown a mortality rate of 29.1 per cent. In 1934 Dr. Stewart reported that the pneumonia mortality rate in hospital practice was still 28 per cent. The authors then conclude that "despite the ever-increasing use of serum and the advent of other newer methods of treatment, such as the oxygen tent, the death rate from lobar pneumonia is essentially what it was a generation ago." I do not feel that this is a fair evaluation of serum therapy. The serum is type-specific, and can be used only for definite types of pneumococcus infection. At the present time its use is limited largely to Type I cases. Therefore, the only accurate measurement of its value is comparison of a group of Type I cases who have received serum with another group of Type I cases who have not received serum. Such figures are now available from the five-year study of the Massachusetts Department of Public Health, and are encouraging. Dr. Heffron reports 406 cases treated in the first four days with the serum with a mortality of 10.1 per cent, while in 177 untreated Type I cases the mortality was 27.1 per cent.

2. In regard to the physiological changes which may be expected from the use of diathermy in pneumonia, the authors have not taken into account the very careful experimental work done by Drs. Binger and Christie at the Rockefeller Institute for Medical Research.* Their experiments on animals and on three human subjects, while perhaps not conclusive, should be given an important place in the consideration of the use of diathermy in pneumonia. After using small thermocouples inserted into the consolidated lung they conclude that the accepted dosage of diathermy does not heat the lung above the temperature prevailing in the rest of the body. This conclusion is at variance with the statement in the article under consideration, which says: "That heat causes dilatation of blood vessels with resulting local hyperemia can readily be observed on the surface of the body when any form of heat is applied to it. It is, therefore, not unreasonable to expect similar changes in deep-seated tissues which are heated by diathermy, namely, the consolidated portions of the lungs in pneumonia."

3. But more important than the question of the value of serum, or the physiological results of diathermy, is an actual analysis of the cases presented in the "control" and the "diathermy" groups. A study of the tables brings out the following points:

   A) The present series (36 cases) is so small that one is not justified in drawing any conclusions as to the effect of diathermy on the mortality rate. This point the authors realize.

   B) Although it was originally intended that the candidates for diathermy were to be alternate cases, in the actual series this plan was not carried out. For instance, from January twentieth through March seventh there were *two treated cases as against nine untreated* cases. In most years the mortality from pneumonia is high during this period, and four deaths occurred in the nine untreated cases.

*Binger, C. A. L. and Christie, R. V.: J. A. M. A. 91: (Aug. 11) 67, 1928.

From March eighth through May first, the time of year when mortality is apt to be lower, there were *ten treated as against two untreated* cases.

C) The age group of the controls is definitely higher than in the treated group, the average age of the controls being thirty-nine years (with only four cases under thirty years of age), whereas the average age in the group treated with diathermy is thirty-two (with ten cases under thirty years of age). Since age is accepted as a significant prognostic factor in pneumonia, this difference would weight the series in favor of the treated group.

D) In comparing the mortality rate in the treated and untreated groups it should be noted that of the six fatal cases in the control group, two had uremia and a third was a chronic alcoholic with delirium tremens and a nonprotein nitrogen of 80 mg. A fourth death was in another chronic alcoholic who had had three previous attacks of pneumonia; and since it occurred thirty days after admission could not be considered a primary pneumonia death. It so happens that the diathermy group does not include any case with so grave a prognosis.

Before drawing any conclusions as to the effect of diathermy on the mortality rate in pneumonia, one must then look for a larger and more carefully alternated series. I realize that the authors are interested primarily in symptomatic relief, but their article does stress an apparent lowering of the mortality rate, and therefore must be evaluated partly on an analysis of the data presented on this point.

Sincerely yours,

DONALD S. KING, M.D.

DR. JOSEPH RESNIK EXPLAINS A CONFUSING SITUATION

December 16, 1935.

Editor, *New England Journal of Medicine*,

Similarity of names and addresses has caused confusion in the minds of some of my medical colleagues. I, therefore, wish to state that I am not connected with any gymnasium or health club, nor do I carry any contract medical work.

Respectfully yours,

JOSEPH RESNIK, M.D.

184 Bay State Road, Boston.

RECENT DEATH

STRONG—THOMAS MORRIS STRONG, M.D., of 56 Penfield Street, Dorchester, died at the Forest Hills Hospital, Jamaica Plain, December 17, 1935. Dr. Strong was born in 1848 in Rosedale, New York, and graduated from Rutgers College in 1868 and from the New York Homeopathic Medical College and Flower Hospital in 1871.

His first practice was at Flint, Michigan, and he was later located at Aurora, New York; Allegheny, Pennsylvania; and Macon, Georgia, before settling in Boston.

For six years he was superintendent of the Massachusetts Memorial Hospitals. His practice was devoted to the eye, ear, and nose with offices at the Hotel Ilkley, Huntington Avenue, Boston. He was treasurer of the Massachusetts Homeopathic Medical Society for twenty-five years and was a member of the American Institute of Homeopathy and the Surgical and Gynecological Society.

He was a Mason and a former member of the Society of Colonial Wars, and the Sons of the American Revolution and the Boston City Club.

His widow, Mrs. Ada M. (Hodgkins) Strong, survives him.

NOTICES

FITCHBURG CANCER CLINIC

There will be a consultation cancer clinic January 8 at the Burbank Hospital, 9 A.M. to 12 P.M. The consultants are Dr. Horatio Rogers, visiting surgeon to the Massachusetts General Hospital and the Pondville Hospital, and Dr. Langdon Parsons, visiting surgeon to the Massachusetts General, the Huntington Memorial, and the Pondville Hospitals.

Hope has been expressed that doctors will take advantage of this opportunity to be present with or refer by note any of their patients having cancer or suspicious of a malignant condition.

FITCHBURG CANCER COMMITTEE,
F. H. THOMPSON, SR., M.D., *Chairman*,
WALTER F. SAWYER, M.D., *Secretary*,
HERVEY B. PITCHER, M.D.,
CHARLES J. LASERTE, M.D.,
ERSKINE R. PICKWICK, M.D.

APPOINTMENT OF DR. C. R. ABBOTT

Dr. Charles R. Abbott of Clinton has been reappointed to the position of Associate Medical Examiner of the fourth Worcester District.

FIRST INTERNATIONAL CONFERENCE ON FEVER THERAPY

The first international meeting on fever therapy will be held in New York City, September, 1936. The use of fever induced by physical and other agencies

as a therapeutic procedure has received universal attention in the past few years. The conference will aim to collect and crystallize available data in this field. Therapeutic, physiological and pathological phases of fever will be discussed.

The suggestion for this conference originated with a group of interested European physicians. Five national conferences have been held in the United States of America. The first three sessions met at Rochester University Medical School in 1931, 1932 and 1933. The fourth assembled at Columbia University College of Physicians and Surgeons in 1934. The fifth was held in 1935 at Miami Valley Hospital, Dayton, Ohio.

It is planned to translate abstracts of all the papers into French, English and German. In order to make the printed copies of the transactions available for the conference, it is necessary that manuscripts and abstracts be submitted not later than June 1, 1936. Those interested in participating are requested to make early application.

Further information concerning the conference may be obtained from the secretary.

BARON HENRI DE ROTHSCHILD, *Chairman*,
Paris, France.
DR. WILLIAM BIERMAN, *Secretary*,
471 Park Avenue,
New York City, U.S.A.

American Committee
DR. A. U. DESJARDINS, *Chairman*.
DR. W. BIERMAN
DR. F. W. HARTMAN
DR. L. E. HINSIE
DR. C. A. NEYMANN
DR. W. M. SIMPSON
DR. S. L. WARREN

THE VAN METER PRIZE

The American Association for the Study of Goiter again offers the Van Meter Prize Award of $300.00 and two honorable mentions for the best essays submitted on the goiter problem. This award will be made at the discretion of the Society at its next annual meeting to be held in Chicago, Illinois, on June 8, 9 and 10.

The competing manuscripts, which should not exceed 3000 words in length, must be presented in English and a typewritten double-spaced copy sent to the Corresponding Secretary, Dr. W. Blair Mosser, 133 Biddle Street, Kane, Pennsylvania, not later than March 1, 1936. Manuscripts received after this date will be held for competition the next year or returned at the author's request.

The Committee that will review the manuscripts is composed of men well known in the fields of research and clinical investigation of problems related to the thyroid gland.

The Association will publish the manuscript receiving the prize award in their annual Proceedings, and reserve a place on the program of the annual meeting for presentation of the manuscript by the author, if it is possible for him to attend.

W. BLAIR MOSSER, M.D., *Corresponding Secretary*.

REMOVAL

WALTER S. LEVENSON, M.D., announces the removal of his office from 371 Commonwealth Avenue, Boston, to 370 Commonwealth Avenue, Boston.

REPORTS AND NOTICES OF MEETINGS

NORFOLK DISTRICT MEDICAL SOCIETY

REPORT OF THE COMMITTEE ON VACCINATIONS, IMMUNIZATIONS AND EXAMINATIONS OF WELL BABIES AND PRESCHOOL CHILDREN

On November 12, 1935, conferences were held with Dr. Francis X. Mahoney, the Health Commissioner of Boston, and Dr. Charles F. Wilinsky, Deputy Commissioner of Health and Director of Child Hygiene and Health Units.

Both were anxious and willing to coöperate in the development of some practical method agreeable to the physicians of Boston which would make possible a greater participation by them in the program of preventive medicine.

They realize fully the economic problems confronting the medical profession and are mindful of the fact that undoubtedly some who come to the clinics of the Health Department can afford to obtain medical services in the offices of the family doctor.

They are mindful, however, that the health of the community is the responsibility of the Health Department and that the expenditures of the city for the maintenance of these services are justifiable and essential and should be continued. They regard these services as educational in their import and serve the doubly useful purpose of not only rendering preventive service but also for the stimulation of the public in a desire for preventive measures.

They are willing to coöperate with the medical profession in an effort to get people who can afford to pay to prefer to obtain the service on an individual basis from their family physician and suggest the development of the following plan:

1. That the County Medical Societies coöperate with the Health Department in the furtherance of health education and the stimulation of the public for greater demands for preventive services.

2. That the Medical Society circularize its members and advise them to set aside certain hours in so far as this is possible for the maintenance of preventive clinics including vaccination against smallpox and typhoid, immunization against diphtheria, examinations of well babies, preschool children, etc.

3. That a reasonable office fee be established not to exceed one dollar per visit for this type of service.

4. That acceptable educational literature sponsored by the County Medical Societies and the

Health Department be drawn up to be mailed by the family physician to his patients stressing the importance of this type of service and the willingness of the family doctor to render the same for his patients.

This plan patiently worked out and developed with sufficient time allowed for the laity to appreciate the advantages of this type of service will eventually result in a majority of people who can afford to pay, preferring to receive this from the family physician leaving the clinics maintained by the Health Department available to those who cannot afford to pay as well as to those who have not been educated as yet to prefer the service from private sources.

On November 18, 1935, a special conference was held at the Beth Israel Hospital. The following were present: Dr. Charles F. Wilinsky, Dr. Channing Frothingham, Dr. Robert L. DeNormandie, Dr. Frank S. Cruickshank, and Dr. Henry M. Landesman.

It was decided to have an official combined meeting of the Committees from the Middlesex South, Suffolk, and Norfolk District Medical Societies with the Health Department officials in December to complete definite workable plans for those members of these Societies who wish to do vaccinations and immunizations for diphtheria and typhoid, examinations of well babies, preschool children, etc.

H. M. Landesman, M.D., *Chairman*,
D. L. Lionberger, M.D.,
John B. Hall, M.D.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

A meeting of the Middlesex East District Medical Society was held at Bear Hill Country Club on November 27, 1935, with Dr. F. O. West of Woburn as presiding officer, and Dr. K. L. Maclachlan of Melrose as secretary.

At an excellent dinner, Dr. Charles E. Mongan, President of the Massachusetts Medical Society, was royally welcomed by all the members of the district society, who were present in large numbers to greet him, as well as the scientific speaker, Dr. Howard M. Clute, who presented a paper on Thyroid Disease.

Dr. Mongan discussed the medical aspect of the Social Security Act, and its disadvantages to the profession. He also presented the fallacies of unemployment insurance particularly as applied to this State, which does not need this legislation, in his opinion. He stated that the proposed act has been sponsored by the social uplift workers without adequately consulting the leaders of the medical profession or getting their advice.

Dr. William R. Morrison, Chairman of the Committee on Arrangements, urged the members to reserve June 8, 9 and 10, for the next Annual Meeting and Dinner in Springfield. He stated that new members of the Society will be particularly welcome, and older members are relied on to show their interest in the meetings and clinics.

FAULKNER HOSPITAL CLINICAL MEETING

The next clinical meeting will be held at the Faulkner Hospital on Thursday, January 2, at 5 P.M. In addition to the usual clinical pathological conference Dr. Maurice B. Strauss will speak on Anemias in Pregnancy.

All physicians are invited.

WORCESTER DISTRICT MEDICAL SOCIETY

The January meeting of the Worcester District Medical Society will be held in Thayer Hall at the Worcester City Hospital, Worcester, Mass., on the evening of Wednesday, January 8, 1936. The full program is as follows:

6:15 P.M. Buffet supper.
7:30 P.M. Business session and scientific program.

(1) Head Injuries—Types and treatment. Dr. Benjamin T. Burley, Worcester.

(2) The Roentgen Diagnosis of Abdominal Aorta. Dr. Philip H. Cook, Worcester.

(3) The Treatment of Epileptics and their Relatives. Dr. Foster L. Vibber, Worcester.

Erwin C. Miller, M.D., *Secretary*.

ST. ELIZABETH'S HOSPITAL

Infantile Paralysis Vaccine Meeting

The next meeting of the Staff of St. Elizabeth's Hospital will take place at the hospital, 736 Cambridge Street (Brighton District), Boston, Friday evening, January 3, 1936, at 8:15 P.M.

PROGRAM

Address by John A. Kolmer, M.D., of Philadelphia, Professor of Medicine, Temple University, and Director of the Research Institute of Cutaneous Medicine.

Subject: Infection, Immunity and Vaccination in Infantile Paralysis.

Discussion to be opened by W. Lloyd Aycock, M.D., Director of the Harvard Infantile Paralysis Commission; Hans Zinsser, M.D., Professor of Bacteriology and Immunology, Harvard University Medical School, and John F. Casey, M.D., Visiting Physician, St. Elizabeth's Hospital.

Physicians and medical students are invited.

NEW ENGLAND HEART ASSOCIATION

The next meeting of the New England Heart Association will be held at the Peter Bent Brigham Hospital, Boston, Mass., Monday, January 6, 1936, at 8:15 P.M.

PROGRAM

I. Business: Consideration of revision of Constitution and By-Laws.

II. Clinical:

1. A Method of Determining Blood Volume. Dr. J. G. Gibson, 2nd.
2. Blood Volume Changes in Congestive Heart Failure. Dr. William Evans.

3. Concerning the Mechanism of Hypertensive Crises. Dr. Michel Pijoan.
4. Hemopericardium as a Cause of Sudden Death. Dr. Marshall N. Fulton.
5. The Early Diagnosis of Aortic Stenosis. Dr. Samuel A. Levine.
6. Aortic Stenosis, Angina Pectoris, and Syncope. Dr. A. W. Contratto.
7. Is Digitalis Present in Body Fluids in Digitalized Patients? Dr. Maurice A. Schnitker.

All members and interested physicians are invited to attend.

JAMES M. FAULKNER, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, DECEMBER 30, 1935

Tuesday, December 31—

2:30 P.M. Pediatric Ward Visit. Massachusetts Eye and Ear Infirmary.

Thursday, January 2—

*5 P.M. Faulkner Hospital Clinical Meeting.

Friday, January 3—

*8:15 P.M. St. Elizabeth's Hospital, Infantile Paralysis Vaccine Meeting, 736 Cambridge Street, Brighton.

Saturday, January 4—

*10-12. Staff rounds at the Peter Bent Brigham Hospital.

Sunday, January 5—

4 P.M. Free Public Lecture, Harvard Medical School, Building D, Longwood Avenue. Cancer, by D. F. Jones, M.D.

*Open to the medical profession.

January 2—Faulkner Hospital Clinical Meeting. See page 1327.

January 3—St. Elizabeth's Hospital, Infantile Paralysis Vaccine Meeting. See page 1327.

January 6—New England Heart Association. See page 1327.

January 8—Fitchburg Cancer Clinic. See page 1325.

January 10—William Harvey Society. 8 P.M., Beth Israel Hospital, Boston.

January 27—Springfield Medical Association.

February 24 to May 16, 1936—International Medical Postgraduate Courses in Berlin. See page 1211, issue of December 12.

September, 1936—First International Conference on Fever Therapy. See page 1325.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH DISTRICT MEDICAL SOCIETY

January 8—Meeting at the Riverside Tavern, Haverhill, at 12:30 P.M.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

January 8—Wednesday. Danvers State Hospital, Hathorne. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Hoskins. Subject to be announced later.

February 5—Council Meeting, Boston.

February 12—Wednesday. Addison Gilbert Hospital, Gloucester. Clinic 5 P.M. Dinner 7 P.M. Speaker and subject to be announced later.

March 4—Wednesday. Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Timothy Leary. Subject: Arteriosclerosis.

April 1—Wednesday. Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Richard H. Overholt of the Lahey Clinic. Subject: Chest Surgery.

May 7—Thursday. Censors' Meeting.

May 13—Wednesday. Annual Meeting. Salem Country Club. Dinner at 7 P.M. Speaker: Dr. Paul White. Subject to be announced later.

R. E. STONE, M.D., Secretary.
88 Lothrop Boulevard, Beverly.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings are held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings to be held at the Bear Hill Golf Club at 12:15 P.M.

January 8, March 11, May 6.

K. L. MACLACHLAN, M.D., Secretary.
1 Bellevue Avenue, Melrose.

NORFOLK DISTRICT MEDICAL SOCIETY

January 23, 1936—Hotel Kenmore at 8 P.M. Subject: "Compulsory Sickness Insurance." Speakers to be announced.

February 25, 1936—Massachusetts Memorial Hospitals at 8 P.M. Papers by the staff.

March 31, 1936—Hotel Kenmore, at 8 P.M. Dr. Benedict F. Boland—"Cauterization of the Cervix Uteri Using Various Electrical Methods." Illustrated with lantern slides.

May, 1936—Annual Meeting. (Place, date and subject to be announced.)

The censors meet for the examination of candidates: May 7, 1936; November 5, 1936.

FRANK S. CRUICKSHANK, M.D., Secretary.
1236 Beacon Street, Brookline.

PLYMOUTH DISTRICT MEDICAL SOCIETY

January 16—Goddard Hospital. Subject and speakers to be announced later.

March 19—Plymouth County Sanatorium, South Hanson.

April 16—Brockton Hospital.

May 21—Lakeville State Sanatorium.

G. A. MOORE, M.D., Secretary.
167 Newbury Street, Brockton.

SUFFOLK DISTRICT MEDICAL SOCIETY

January 29, 1936—Joint Meeting with the Boston Medical Library at 8 Fenway. "Observations Around the World," Dr. Walter B. Cannon.

March 18, 1936—Meeting at the Boston Medical Library. "The Laboratory and Clinical Story of Fatigue," Dr. Arlie V. Bock and Dr. David B. Dill. Discussion: Dr. Donald J. MacPherson and Dr. Augustus Thorndike, Jr.

April 29, 1936—Annual Meeting at the Boston Medical Library. "The Treatment of Septicaemia," Dr. Champ Lyons. "The Pleurality of Scarlatinal Streptococcus Toxin," Dr. Sanford B. Hooker. Discussion: Dr. Hans Zinsser.

The medical profession is cordially invited to attend all of these meetings.

ROBERT L. DeNORMANDIE, M.D., President,
CHARLES C. LUND, M.D., Secretary,
FRANCIS T. HUNTER, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

January 8—See page 1327.

February 12, 1936—Wednesday evening. Worcester State Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

March 11, 1936—Wednesday evening. Memorial Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

April 8, 1936—Wednesday evening. Hahnemann Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

May 13, 1936—Wednesday afternoon and evening. Annual Meeting of Society. Time, place and details of program to be announced in an April issue of the Journal.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester.